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   (FILE 'HOME' ENTERED AT 16:08:07 ON 09 OCT 2002)

     FILE 'BIOSIS, CABA, CAPLUS, EMBASE, LIFESCI, MEDLINE, SCISEARCH,
     USPATFULL, JAPIO' ENTERED AT 16:08:23 ON 09 OCT 2002
L1         14339 S PILI
L2           179 S PAPH
L3            98 S L2 AND (MUTAT? OR DELET? OR TRUCAT? OR INSERT? OR MUTAGENESI
L4            21 S L1 AND FOREIGN EPITOPES
L5             1 S L2 AND FOREIGN EPITOPES
L6            90 DUP REM L3 (8 DUPLICATES REMOVED)
L7            18 DUP REM L4 (3 DUPLICATES REMOVED)
L8             1 S L7 AND PAPA
L9          3245 S PAPA
L10            3 S L9 AND FOREIGN EPITOPES
L11            0 S OHANLEY, PETER/AU
L12           24 S HANLEY, PETER/AU
L13           23 DUP REM L12 (1 DUPLICATE REMOVED)
L14            0 S OHANLEY, PETER/AU
L15           13 S DENICH, KENNETH/AU
L16           11 DUP REM L15 (2 DUPLICATES REMOVED)

     FILE 'STNGUIDE' ENTERED AT 16:19:37 ON 09 OCT 2002
L17            0 S L3   AND PAPA

     FILE 'BIOSIS, CABA, CAPLUS, EMBASE, LIFESCI, MEDLINE, SCISEARCH,
     USPATFULL, JAPIO' ENTERED AT 16:21:34 ON 09 OCT 2002
L18           21 S L3 AND PAPA
L19           18 DUP REM L18 (3 DUPLICATES REMOVED)
L20            1 S L19 AND FOREIGN EPITOPES
L21           16 S SCHMIDT, ALEXANDER/AU
L22           14 DUP REM L21 (2 DUPLICATES REMOVED)
L23            0 S L22 AND PILI
L24            0 S M SCHMIDT ALEXANDER/AU

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19 ANSWER 1 OF 18 USPATFULL
AB A method of producing pili and vaccines containing pili are described using bacteria that express at least one immunogenic peptide in a **PapA** region that does not normally contain such a peptide.
AN 2002:258441 USPATFULL
TI Immunogenic pili presenting foreign peptides, their production and use
IN O'Hanley, Peter, Washington, DC, UNITED STATES
Denich, Kenneth, Edmonton, CANADA
Schmidt, M. Alexander, Muenster, GERMANY, FEDERAL REPUBLIC OF
PI US 2002142008 A1 20021003
AI US 2001-833079 A1 20010412 (9)
PRAI US 2000-196491P 20000412 (60)
DT Utility
FS APPLICATION
LREP FOLEY AND LARDNER, SUITE 500, 3000 K STREET NW, WASHINGTON, DC, 20007
CLMN Number of Claims: 7
ECL Exemplary Claim: 1
DRWN 5 Drawing Page(s)
LN.CNT 967

L19 ANSWER 2 OF 18 USPATFULL
AB The present invention relates to novel genes located in two chromosomal regions within uropathogenic E. coli that are associated with virulence. These chromosomal regions are known as pathogenicity islands (PAIs). In particular, the present application discloses 142 sequenced fragments (contigs) of DNA from two pools of cosmids covering pathogenicity islands PAI IV and PAI V located on the chromosome of the uropathogenic Escherichia coli J96. Further disclosed are 351 predicted protein-coding open reading frames within the sequenced fragments.
AN 2002:141608 USPATFULL
TI Nucleotide sequence of Escherichia coli pathogenicity islands
IN Dillon, Patrick J., Carlsbad, CA, UNITED STATES
Choi, Gil H., Rockville, MD, UNITED STATES
Welch, Rodney A., Madison, WI, UNITED STATES
PA Human Genome Sciences, Inc., Rockville, MD, UNITED STATES (U.S. corporation)
PI US 2002072595 A1 20020613
AI US 2001-956004 A1 20010920 (9)
RLI Division of Ser. No. US 1997-976259, filed on 21 Nov 1997, GRANTED, Pat. No. US 6316609
PRAI US 1997-61953P 19971014 (60)
US 1996-31626P 19961122 (60)
DT Utility
FS APPLICATION
LREP HUMAN GENOME SCIENCES INC, 9410 KEY WEST AVENUE, ROCKVILLE, MD, 20850
CLMN Number of Claims: 33
ECL Exemplary Claim: 1
DRWN 2 Drawing Page(s)
LN.CNT 8481
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L19 ANSWER 3 OF 18 USPATFULL
AB A method of producing pili and vaccines containing pili is described using bacteria harboring **mutations** that facilitate detachment of pili from the bacteria. Wild type pili have known immunoprotective effects in treating urinary tract infections. The mutant pili produced by this method are also shown to have such immunoprotective effects. Therefore, the pili may be used to make vaccines for treating urinary tract infections.
AN 2002:105686 USPATFULL
TI Dissociated pili, their production and use
IN O'Hanley, Peter, Washington, DC, UNITED STATES
Denich, Kenneth, Edmonton, CANADA
PI US 2002054888 A1 20020509

AI US 2001-833067 A1 20010412 (9)
PRAI US 2000-196493P 20000412 (60)
DT Utility
FS APPLICATION
LREP Stephen B. Maebius, FOLEY & LARDNER, Suite 500, 3000 K Street, N.W., Washington, DC, 20007-5109
CLMN Number of Claims: 5
ECL Exemplary Claim: 1
DRWN 8 Drawing Page(s)
LN.CNT 727

L19 ANSWER 4 OF 18 USPATFULL
AB Novel methods for the treatment and/or prophylaxis of diseases caused by tissue-adhering bacteria are disclosed. By interacting with periplasmic molecular chaperones it is achieved that the assembly of pili is prevented or inhibited and thereby the infectivity of the bacteria is diminished. Also disclosed are methods for screening for drugs as well as methods for the de novo design of such drugs, methods which rely on novel computer drug modelling methods involving an approximative calculation of binding free energy between macromolecules. Finally, novel pyranosides which are believed to be capable of interacting with periplasmic molecular chaperones are also disclosed.
AN 2002:85159 USPATFULL
TI Treatment or prophylaxis of diseases caused by pilus-forming bacteria
IN Hultgren, Scott, Ballwin, MO, UNITED STATES
Kuehn, Meta, Berkeley, CA, UNITED STATES
Xu, Zheng, Blue Bell, PA, UNITED STATES
Ogg, Derek, Stockholm, SWEDEN
Harris, Mark, Uppsala, SWEDEN
Lepisto, Matti, Lund, SWEDEN
Jones, Charles Hal, Saint Louis, MO, UNITED STATES
Kihlberg, Jan, Dalby, SWEDEN
PI US 2002045199 A1 20020418
AI US 2001-799540 A1 20010307 (9)
RLI Division of Ser. No. US 1996-640877, filed on 10 Oct 1996, PENDING
Division of Ser. No. WO 1994-US13455, filed on 18 Nov 1994, UNKNOWN
Continuation-in-part of Ser. No. US 1993-154035, filed on 18 Nov 1993, ABANDONED
DT Utility
FS APPLICATION
LREP Teresa Stanek Rea, Esq., BURNS, DOANE, SWECKER & MATHIS, L.L.P., P.O. Box 1404, Alexandria, VA, 22313-1404
CLMN Number of Claims: 37
ECL Exemplary Claim: 1
DRWN 25 Drawing Page(s)
LN.CNT 5601
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L19 ANSWER 5 OF 18 USPATFULL
AB Novel methods for the treatment and/or prophylaxis of diseases caused by tissue-adhering bacteria are disclosed. By interacting with periplasmic molecular chaperones it is achieved that the assembly of pili is prevented or inhibited and thereby the infectivity of the bacteria is diminished. Also disclosed are methods for screening for drugs as well as methods for the de novo design of such drugs, methods which rely on novel computer drug modelling methods involving an approximative calculation of binding free energy between macromolecules. Finally, novel pyranosides which are believed to be capable of interacting with periplasmic molecular chaperones are also disclosed.
AN 2002:60940 USPATFULL
TI Treatment or prophylaxis of diseases caused by pilus-forming bacteria
IN Hultgren, Scott, Ballwin, MO, UNITED STATES
Kuehn, Meta, Berkeley, CA, UNITED STATES
Xu, Zheng, Blue Bell, PA, UNITED STATES

Ogg, Derek, Stockholm, SWEDEN
Harris, Mark, Uppsala, SWEDEN
Lepisto, Matti, Lund, SWEDEN
Jones, Charles Hal, Saint Louis, MO, UNITED STATES
Kihlberg, Jan, Dalby, SWEDEN
PI US 2002034774 A1 20020321
AI US 2001-799576 A1 20010307 (9)
RLI Division of Ser. No. US 1996-640877, filed on 10 Oct 1996, PENDING
Division of Ser. No. WO 1994-US13455, filed on 18 Nov 1994, UNKNOWN
Continuation-in-part of Ser. No. US 1993-154035, filed on 18 Nov 1993, ABANDONED
DT Utility
FS APPLICATION
LREP Teresa Stanek Rea, Esq., BURNS, DOANE, SWECKER & MATHIS, L.L.P., P.O. Box 1404, Alexandria, VA, 22313-1404
CLMN Number of Claims: 37
ECL Exemplary Claim: 1
DRWN 25 Drawing Page(s)
LN.CNT 5543
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L19 ANSWER 6 OF 18 USPATFULL
AB The sequences of nucleic acids encoding proteins required for E. coli proliferation are disclosed. The nucleic acids can also be used to screen for homologous genes that are required for proliferation in microorganisms other than E. coli. The nucleic acids can also be used to design expression vectors and secretion vectors. The nucleic acids can be used to express proteins or portions thereof, to obtain antibodies capable of specifically binding to the expressed proteins, and to use those expressed proteins as a screen to isolate candidate molecules for rational drug discovery programs. The nucleic acids of the present invention can also be used in various assay systems to screen for antimicrobial agents.
AN 2002:37998 USPATFULL
TI Genes identified as required for proliferation of E. coli
IN Forsyth, R. Allyn, San Diego, CA, UNITED STATES
Ohlsen, Kari L., San Diego, CA, UNITED STATES
Zyskind, Judith W., La Jolla, CA, UNITED STATES
PI US 2002022718 A1 20020221
AI US 2000-741669 A1 20001219 (9)
PRAI US 1999-173005P 19991223 (60)
DT Utility
FS APPLICATION
LREP KNOBBE MARTENS OLSON & BEAR LLP, 620 NEWPORT CENTER DRIVE, SIXTEENTH FLOOR, NEWPORT BEACH, CA, 92660
CLMN Number of Claims: 131
ECL Exemplary Claim: 1
DRWN 3 Drawing Page(s)
LN.CNT 5270
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L19 ANSWER 7 OF 18 USPATFULL
AB Novel methods for the treatment and/or prophylaxis of diseases caused by tissue-adhering bacteria are disclosed. By interacting with periplasmic molecular chaperones it is achieved that the assembly of pili is prevented or inhibited and thereby the infectivity of the bacteria is diminished. Also disclosed are methods for screening for drugs as well as methods for the de novo design of such drugs, methods which rely on novel computer drug modelling methods involving an approximative calculation of binding free energy between macromolecules. Finally, novel pyranosides which are believed to be capable of interacting with periplasmic molecular chaperones are also disclosed.
AN 2002:174960 USPATFULL
TI Compounds and pharmaceutical compositions for the treatment and

prophylaxis of bacterial infections
IN Hultgren, Scott, Ballwin, MO, United States
Kuehn, Meta, Berkeley, CA, United States
Xu, Zheng, Blue Bell, PA, United States
Ogg, Derek, Uppsala, SWEDEN
Harris, Mark, Uppsala, SWEDEN
Lepisto, Matti, Lund, SWEDEN
Jones, Charles Hal, Saint Louis, MO, United States
Kihlberg, Jan, Dalby, SWEDEN
PA Washington University, St. Louis, MO, United States (U.S. corporation)
Siga Pharmaceuticals, Inc., Corvallis, OR, United States (U.S. corporation)
PI US 6420127 B1 20020716
WO 9514028 19950526
AI US 1996-640877 19961010 (8)
WO 1994-US13455 19941118
19961010 PCT 371 date
DT Utility
FS GRANTED
EXNAM Primary Examiner: Swartz, Rodney P
LREP Burns, Doane, Swecker & Mathis, L.L.P.
CLMN Number of Claims: 9
ECL Exemplary Claim: 1
DRWN 35 Drawing Figure(s); 25 Drawing Page(s)
LN.CNT 5398
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L19 ANSWER 8 OF 18 CAPLUS COPYRIGHT 2002 ACS
AB A the authors disclose the prepn. and isolation of pili from Escherichia coli with **deletional mutations** in **papH**. In a mouse model of pyelonephritis, vaccination with these pili prevented renal colonization. In **addn**., the authors disclose epitopes of **papA** and the use of these immunogenic peptide in a **PapA** region that does not normally contain such a peptide.
AN 2001:780956 CAPLUS
DN 135:343274
TI Immunogenic pili presenting foreign peptides: vaccination against urinary tract infections
IN Denich, Kenneth; Schmidt, M. Alexander
PA O'Hanley, Peter, USA
SO PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001079277	A2	20011025	WO 2001-US11918	20010412
	WO 2001079277	A3	20020523		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 2002142008	A1	20021003	US 2001-833079	20010412
PRAI	US 2000-196491P	P	20000412		

L19 ANSWER 9 OF 18 USPATFULL
AB The present invention relates to novel genes located in two chromosomal regions within uropathogenic E. coli that are associated with virulence.

These chromosomal regions are known as pathogenicity islands (PAIs). In particular, the present application discloses 142 sequenced fragments (contigs) of DNA from two pools of cosmids covering pathogenicity islands PAI IV and PAI V located on the chromosome of the uropathogenic Escherichia coli J96. Further disclosed are 351 predicted protein-coding open reading frames within the sequenced fragments.

AN 2001:202784 USPATFULL
TI Nucleotide sequence of Escherichia coli pathogenicity islands
IN Dillon, Patrick J., Gaithersburg, MD, United States
Choi, Gil H., Rockville, MD, United States
Welch, Rodney A., Madison, WI, United States
PA Human Genome Sciences, Inc., Rockville, MD, United States (U.S. corporation)
Wisconsin Alumni Research Foundation, Madison, WI, United States (U.S. corporation)
PI US 6316609 B1 20011113
AI US 1997-976259 19971121 (8)
PRAI US 1997-61953P 19971014 (60)
US 1996-31626P 19961122 (60)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Clark, Deborah J. R.; Assistant Examiner: Sorbello, Eleanor
LREP Human Genome Sciences, Inc.
CLMN Number of Claims: 113
ECL Exemplary Claim: 1
DRWN 2 Drawing Figure(s); 2 Drawing Page(s)
LN.CNT 3533
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L19 ANSWER 10 OF 18 USPATFULL
AB An antigen which, as its major immunizing component, comprises a determinant of an adhesin polypeptide or an immunogenically active subsequence thereof or a precursor therefor which is convertible to an immunogenically active form, antibodies against which determinant react with the adhesin polypeptide produced by pathogenic adhesin-forming bacteria which adhere to mammalian tissue, antibodies against such antigen, and DNA expressing, as a principal gene product thereof, such antigen.

AN 2001:158467 USPATFULL
TI Anti-bodies binding adhesin-derived antigens
IN Lindberg, Frederik Carl, Sandviken, Sweden
Lund, Bjorn Olof, Umea, Sweden
Baga, Britt Monika, Umea, Sweden
Norgen, Mari Elisabet, Umea, Sweden
Goransson, Mikael, Umea, Sweden
Uhlin, Bernt Eric, Umea, Sweden
Normark, Jan Staffan, Holmsund, Sweden
Lark, David Lee, Umea, Sweden
PA Symbicom Aktiebolag, Umea, Sweden (non-U.S. corporation)
PI US 6291649 B1 20010918
AI US 1998-75396 19980511 (9)
RLI Division of Ser. No. US 1995-447685, filed on 23 May 1995, now patented, Pat. No. US 5804198 Continuation of Ser. No. US 1993-123032, filed on 20 Sep 1993, now abandoned Continuation of Ser. No. US 1992-856829, filed on 23 Mar 1992, now abandoned Continuation of Ser. No. US 1991-678167, filed on 28 Mar 1991, now abandoned Continuation of Ser. No. US 1988-245469, filed on 16 Sep 1988, now abandoned Continuation of Ser. No. US 817849
PRAI DK 1984-2190 19840502
DT Utility
FS GRANTED
EXNAM Primary Examiner: Graser, Jennifer E.
LREP Cooper, Iver P.

CLMN Number of Claims: 45
ECL Exemplary Claim: 1
DRWN 3 Drawing Figure(s); 3 Drawing Page(s)
LN.CNT 2145
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L19 ANSWER 11 OF 18 CAPLUS COPYRIGHT 2002 ACS
AB Uropathogenic Escherichia coli is the leading cause of urinary tract infection and hospital visits in North America. Cystitis and acute pyelonephritis, infection of the bladder and kidney, resp., are the two most common syndromes encountered in patients with urinary tract infection. The authors sequenced and annotated 71,684 bases of a previously unidentified pathogenicity-assocd. island (PAI) from E. coli strain CFT073. This PAI contained 89 open-reading frames encoding a pap operon, iron-regulated genes, mobile genetic elements, and a large proportion of unknown or unidentified open-reading frames. Dot blot anal. with 11 DNA sequences from this PAI demonstrated that 7 sequences were more prevalent among uropathogens: 2 probes were more prevalent among cystitis and pyelonephritis isolates, 2 among pyelonephritis isolates only, and 3 among cystitis isolates only than among fecal isolates. These data suggest that groups of uropathogens have genetic differences that may be responsible for the different clin. outcomes.
AN 2001:801427 CAPLUS
DN 137:1175
TI Identification of DNA sequences from a second pathogenicity island of uropathogenic Escherichia coli CFT073: Probes specific for uropathogenic populations
AU Rasko, David A.; Phillips, Jill A.; Li, Xin; Mobley, Harry L. T.
CS Department of Microbiology and Imnunology, University of Maryland School of Medicine, Baltimore, MD, 21201, USA
SO Journal of Infectious Diseases (2001), 184(8), 1041-1049
CODEN: JIDIAQ; ISSN: 0022-1899
PB University of Chicago Press
DT Journal
LA English
RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 12 OF 18 USPATFULL
AB Novel methods for the treatment and/or prophylaxis of diseases caused by tissue-adhering bacteria are disclosed. By interacting with periplasmic molecular chaperones it is achieved that the assembly of pili is prevented or inhibited and thereby the infectivity of the bacteria is diminished. Also disclosed are methods for screening for drugs as well as methods for the de novo design of such drugs, methods which rely on novel computer drug modelling methods involving an approximative calculation of binding free energy between macromolecules. Finally, novel pyranosides which are believed to be capable of interacting with periplasmic molecular chaperones are also disclosed.
AN 2000:160793 USPATFULL
TI Treatment or prophylaxis of diseases caused by pilus-forming bacteria
IN Hultgren, Scott, Ballwin, MO, United States
Kuehn, Meta, Berkeley, CA, United States
Xu, Zheng, Blue Bell, PA, United States
Ogg, Derek, Uppsala, Sweden
Harris, Mark, Uppsala, Sweden
Lepisto , Matti, Lund, Sweden
Kihlberg, Jan, Dalby, Sweden
Jones, Charles Hal, St. Louis, MO, United States
PA SIGA Pharmaceuticals, Inc., New York, NY, United States (U.S. corporation)
Washington University, St. Louis, MO, United States (U.S. corporation)
PI US 6153396 20001128
AI US 1995-465275 19950605 (8)

RLI Division of Ser. No. WO 1994-US13455, filed on 18 Nov 1994 which is a continuation-in-part of Ser. No. US 1993-154035, filed on 18 Nov 1993, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Swartz, Rodney P.
LREP Burns, Doane, Swecker & Mathis, L.L.P.
CLMN Number of Claims: 10
ECL Exemplary Claim: 1
DRWN 29 Drawing Figure(s); 24 Drawing Page(s)
LN.CNT 5410
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L19 ANSWER 13 OF 18 USPATFULL
AB Novel methods for the treatment and/or prophylaxis of diseases caused by tissue-adhering bacteria are disclosed. By interacting with periplasmic molecular chaperones it is achieved that the assembly of pili is prevented or inhibited and thereby the infectivity of the bacteria is diminished. Also disclosed are methods for screening for drugs as well as methods for the de novo design of such drugs, methods which rely on novel computer drug modelling methods involving an approximative calculation of binding free energy between macromolecules. Finally, novel pyranosides which are believed to be capable of interacting with periplasmic molecular chaperones are also disclosed.
AN 1999:163678 USPATFULL
TI Treatment or prophylaxis of diseases caused by pilus-forming bacteria
IN Hultgren, Scott, 1637 Country Hill La., Ballwin, MO, United States
Kuehn, Meta, 7351 Claremont Ave., #2, Berkeley, CA, United States 94705
Xu, Zheng, 887 Village Cir., Blue Bell, PA, United States 19422
Ogg, Derek, Artillerigatan 16B, S-752 37, Uppsala, Sweden
Harris, Mark, Norbykallvagen 2, S-756 45 Uppsala, Sweden
Lepisto , Matti, Flygelvaagen 257, S-224 73 Lund, Sweden
Kihlberg, Jan, Havrevagen 16, S-240 10 Dalby, Sweden
Jones, Charles Hal, 1104 Moorlands Dr., St. Louis, MO, United States 63110
PI US 6001823 19991214
AI US 1995-462436 19950605 (8)
RLI Division of Ser. No. WO 1994-US13455, filed on 18 Nov 1994 which is a continuation-in-part of Ser. No. US 1993-154035, filed on 18 Nov 1993, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Raymond, Richard L.
LREP Burns, Doane, Swecker & Mathis, L.L.P.
CLMN Number of Claims: 5
ECL Exemplary Claim: 1
DRWN 34 Drawing Figure(s); 24 Drawing Page(s)
LN.CNT 5409
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L19 ANSWER 14 OF 18 USPATFULL
AB An antigen which, as its major immunizing component, comprises a determinant of an adhesin polypeptide or an immunogenically active subsequence thereof or a precursor therefor which is convertible to an immunogenically active form, antibodies against which determinant react with the adhesin polypeptide produced by pathogenic adhesin-forming bacteria which adhere to mammalian tissue, antibodies against such antigen, and DNA expressing, as a principal gene product thereof, such antigen.
AN 1998:108037 USPATFULL
TI Vaccines against disease caused by pathogenic pilus-forming bacteria
IN Lindberg, Frederik Carl, Sandviken, Sweden
Lund, Bjorn Olof, Ume.ang., Sweden
B.ang.ga, Britt Monika, Ume.ang., Sweden

Norgren, Mari Elisabet, Ume.ang., Sweden
Goransson, Mikael, Ume.ang., Sweden
Uhlin, Bernt Eric, Ume.ang., Sweden
Normark, Jan Staffan, Holmsund, Sweden
Lark, David Lee, Ume.ang., Sweden
PA Symbicom Aktiebolag, Umea, Sweden (non-U.S. corporation)
PI US 5804198 19980908
AI US 1995-447685 19950523 (8)
RLI Continuation of Ser. No. US 1993-123032, filed on 20 Sep 1993, now abandoned which is a continuation of Ser. No. US 1992-856829, filed on 23 Mar 1992, now abandoned which is a continuation of Ser. No. US 1991-678167, filed on 28 Mar 1991, now abandoned which is a continuation of Ser. No. US 1988-245469, filed on 16 Sep 1988, now abandoned which is a division of Ser. No. US 1986-817849, filed on 19 Feb 1986, now patented, Pat. No. US 4795803
PRAI DK 1984-2190 19840502
DT Utility
FS Granted
EXNAM Primary Examiner: Sidberry, Hazel F.
LREP Cooer, Iver P.
CLMN Number of Claims: 38
ECL Exemplary Claim: 1
DRWN 3 Drawing Figure(s); 3 Drawing Page(s)
LN.CNT 2188
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L19 ANSWER 15 OF 18 MEDLINE
AB The papJ gene of uropathogenic Escherichia coli is required to maintain the integrity of Gal alpha (1-4)Gal-binding P pili. Electron microscopy and ELISA have established that strains carrying the papJ1 mutant allele have a large amount of pilus antigen free of the cells. In contrast to the whole pili released by strains unable to produce the **PapH** pilus anchor, the free papJ1 pili consist of variably sized segments that appear to result from internal breakages to the pilus. The DNA sequence of papJ is presented and its gene product identified as an 18kD periplasmic protein that possesses homology with nucleotide-binding proteins. PapJ may function as a 'molecular chaperone' directly or indirectly establishing the correct assembly of **PapA** subunits in the P pilus.
AN 90355835 MEDLINE
DN 90355835 PubMed ID: 1975085
TI Integrity of Escherichia coli P pili during biogenesis: properties and role of PapJ.
AU Tennent J M; Lindberg F; Normark S
CS Department of Microbiology, University of Umea, Sweden.
SO MOLECULAR MICROBIOLOGY, (1990 May) 4 (5) 747-58.
Journal code: 8712028. ISSN: 0950-382X.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-X51704
EM 199009
ED Entered STN: 19901026
Last Updated on STN: 19990129
Entered Medline: 19900927

L19 ANSWER 16 OF 18 USPATFULL
AB An antigen which, as its major immunizing component, comprises a determinant of an adhesin polypeptide or an immunogenically active subsequence thereof or a precursor therefor which is convertible to an immunogenically active form, antibodies against which determinant react with the adhesion polypeptide produced by pathogenic adhesin-forming bacteria which adhere to mammalian tissue, antibodies against such antigen, and DNA expressing, as a principal gene product thereof, such

antigen.
AN 89:1283 USPATFULL
TI Adhesin antigens, antibodies and DNA fragment encoding the antigen, methods and means for diagnosis and immunization etc.
IN Lindberg, Frederick C., Sandviken, Sweden
Lund, Bjorn O., Umea, Sweden
Baga, Britt M., Umea, Sweden
Norgren, Mari E., Umea, Sweden
Goransson, Mikael, Umea, Sweden
Uhlin, Bernt E., Umea, Sweden
Normark, Jan S., Holmsund, Sweden
Lark, David L., Umea, Sweden
PA Syn-Tek AB, Umea, Sweden (non-U.S. corporation)
PI US 4795803 19890103
WO 8505037 19851121
AI US 1986-817849 19860219 (6)
WO 1985-DK45 19850502
19860219 PCT 371 date
19860219 PCT 102(e) date
PRAI DK 1984-2190 19840502
DT Utility
FS Granted
EXNAM Primary Examiner: Warden, Robert J.; Assistant Examiner: Saunders, David A.
LREP White, John P.
CLMN Number of Claims: 10
ECL Exemplary Claim: 1
DRWN 3 Drawing Figure(s); 3 Drawing Page(s)
LN.CNT 1912
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L19 ANSWER 17 OF 18 MEDLINE
AB E. coli expressing the **papA**-I genes produce pili that mediate specific adhesion to mammalian cells. We show that the major pilus subunit gene, **papA**, is part of a polycistronic transcriptional unit subject to specific posttranscriptional processing. A primary transcript also encoding the papB regulatory gene product is endonucleolytically cleaved, resulting in the rapid decay of the papB-encoding 5' half of the mRNA, whereas the **papA**-encoding 3' half remains as a quite stable transcript. Processing and differential mRNA stability thereby result in accumulation of mRNAs encoding only the major pilus subunit. A sequence immediately downstream of the **papA** coding region may serve as a stability determinant for the **papA** transcript and concomitantly attenuate read-through transcription into the minor pilus subunit gene **papH**. This suggests that differential expression of genes within an operon may include endo- and exonucleolytic processing of the mRNA.
AN 88135752 MEDLINE
DN 88135752 PubMed ID: 2449283
TI Processed mRNA with differential stability in the regulation of E. coli pilin gene expression.
AU Baga M; Goransson M; Normark S; Uhlin B E
CS Department of Microbiology, University of Umea, Sweden.
SO CELL, (1988 Jan 29) 52 (2) 197-206.
Journal code: 0413066. ISSN: 0092-8674.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198804
ED Entered STN: 19900308
Last Updated on STN: 19990129
Entered Medline: 19880407

L19 ANSWER 18 OF 18 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 1

AB The biogenesis of Escherichia coli Pap pili, encoded by the pap gene cluster, was studied. A novel gene, **papH**, was identified and found to encode a weakly expressed pilin-like protein. **PapH** was dispensable for digalactoside-specific binding and for formation of Pap pili. However, in **papH deletion** mutants 50%-70% of total pilus antigen was found free of the cells. We present evidence showing coregulation of **papH** and the adjacent gene, **papA**, which encodes the major pilin subunit. A decrease in the **PapA** to **PapH** ratio resulted in a large fraction of cells producing shortened pili, whereas overproduction of **PapA** relative to **PapH** resulted in cells with lengthened pili. The data show that **PapH** has roles in anchoring the pilus to the cell and in modulating pilus length.

AN 1988:422032 BIOSIS

DN BA86:84644

TI BIOGENESIS OF ESCHERICHIA-COLI PAP PILI **PAPH** A MINOR PILIN SUBUNIT INVOLVED IN CELL ANCHORING AND LENGTH MODULATION.

AU BAGA M; NORGREN M; NORMARK S

CS DEP. MICROBIOL., UNIV. UMEA, S-901 87 UMEA, SWEDEN.

SO CELL, (1987) 49 (2), 241-252.
CODEN: CELLB5. ISSN: 0092-8674.

FS BA; OLD

LA English

=>

ANSWER 1 OF 11 USPATFULL

AB A method of producing pili and vaccines containing pili are described using bacteria that express at least one immunogenic peptide in a PapA region that does not normally contain such a peptide.

AN 2002:258441 USPATFULL

TI Immunogenic pili presenting foreign peptides, their production and use

IN O'Hanley, Peter, Washington, DC, UNITED STATES
Denich, Kenneth, Edmonton, CANADA
Schmidt, M. Alexander, Muenster, GERMANY, FEDERAL REPUBLIC OF

PI US 2002142008 A1 20021003

AI US 2001-833079 A1 20010412 (9)

PRAI US 2000-196491P 20000412 (60)

DT Utility

FS APPLICATION

LREP FOLEY AND LARDNER, SUITE 500, 3000 K STREET NW, WASHINGTON, DC, 20007

CLMN Number of Claims: 7

ECL Exemplary Claim: 1

DRWN 5 Drawing Page(s)

LN.CNT 967

L16 ANSWER 2 OF 11 USPATFULL

AB A method of producing pili and vaccines containing pili is described using bacteria harboring mutations that facilitate detachment of pili from the bacteria. Wild type pili have known immunoprotective effects in treating urinary tract infections. The mutant pili produced by this method are also shown to have such immunoprotective effects. Therefore, the pili may be used to make vaccines for treating urinary tract infections.

AN 2002:105686 USPATFULL

TI Dissociated pili, their production and use

IN O'Hanley, Peter, Washington, DC, UNITED STATES
Denich, Kenneth, Edmonton, CANADA

PI US 2002054888 A1 20020509

AI US 2001-833067 A1 20010412 (9)

PRAI US 2000-196493P 20000412 (60)

DT Utility

FS APPLICATION

LREP Stephen B. Maebius, FOLEY & LARDNER, Suite 500, 3000 K Street, N.W., Washington, DC, 20007-5109

CLMN Number of Claims: 5

ECL Exemplary Claim: 1

DRWN 8 Drawing Page(s)

LN.CNT 727

L16 ANSWER 3 OF 11 USPATFULL

AB The present invention is for improved methods of inactivating viruses in a sample by exposing the sample to a combination of pressure treatment and exposure to an inactivating agent. The sample can be repeatedly cycled between relatively high and low pressures and the inactivating agent is selected from ethyleneimine, ethyleneimine oligomers, psoralens, DNase and RNase.

AN 2002:27091 USPATFULL

TI Methods for inactivating viruses

IN Setcavage, Thomas M., Milford, NJ, UNITED STATES
Denich, Kenneth, Edmonton, CANADA

PI US 2002015937 A1 20020207

AI US 2001-774294 A1 20010129 (9)

PRAI US 2000-179230P 20000131 (60)

DT Utility

FS APPLICATION

LREP BELL, BOYD & LLOYD LLC, P.O. Box 1135, Chicago, IL, 60690-1135

CLMN Number of Claims: 20

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 570
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L16 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2002 ACS
AB A the authors disclose the prepn. and isolation of pili from Escherichia coli with deletional mutations in papH. In a mouse model of pyelonephritis, vaccination with these pili prevented renal colonization. In addn., the authors disclose epitopes of papA and the use of these immunogenic peptide in a PapA region that does not normally contain such a peptide.
AN 2001:780956 CAPLUS
DN 135:343274
TI Immunogenic pili presenting foreign peptides: vaccination against urinary tract infections
IN **Denich, Kenneth**; Schmidt, M. Alexander
PA O'Hanley, Peter, USA
SO PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001079277	A2	20011025	WO 2001-US11918	20010412
	WO 2001079277	A3	20020523		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 2002142008	A1	20021003	US 2001-833079	20010412
PRAI	US 2000-196491P	P	20000412		

L16 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2002 ACS
AB A method of producing pili and vaccines containing pili is described using bacteria harboring mutations that facilitate detachment of pili from the bacteria. Wild type pili have known immunoprotective effects in treating urinary tract infections. The mutant pili produced by this method are also shown to have such immunoprotective effects. Therefore, the pili may be used to make vaccines for treating urinary tract infections.
AN 2001:776594 CAPLUS
TI Dissociated pili, their production and use
IN **Denich, Kenneth**
PA O'hanley, Peter, USA
SO PCT Int. Appl.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001078773	A2	20011025	WO 2001-US11919	20010412
	WO 2001078773	A3	20020207		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,				

DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2002054888 A1 20020509 US 2001-833067 20010412

PRAI US 2000-196493P P 20000412

L16 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2002 ACS

AB The present invention is for improved methods of inactivating viruses in a sample by exposing the sample to a combination of pressure treatment and exposure to an inactivating agent. The sample can be repeatedly cycled between relatively high and low pressures and the inactivating agent is selected from ethyleneimine, ethyleneimine oligomers, psoralens, DNase and RNase.

AN 2001:565233 CAPLUS

DN 135:134611

TI Methods for inactivating viruses

IN Setcavage, Thomas M.; **Denich, Kenneth**

PA Consortium for Plasma Science, LLC, USA

SO PCT Int. Appl., 33 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001055354	A1	20010802	WO 2001-US2955	20010129

W: AU, CA, JP

RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR

US 2002015937 A1 20020207 US 2001-774294 20010129

PRAI US 2000-179230P P 20000131

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 7 OF 11 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 1

AB Cytokines are potentially useful in vaccination as adjuvants or modulators of the type of response induced. The work below describes the expression of a cloned cytokine gene for murine interleukin-4 (mIL-4) by a live vaccine vector, an attenuated aroA strain (SL7207) of Salmonella typhimurium, in a murine model system. SL7207 was used as a carrier for two different high-level expression vectors. Both resulting strains, designated SL7207(pOmpAmIL-4) and SL7207(pKKmIL-4), expressed the cloned gene product as monitored by both immunological and biological assays. However, SL7207(pOmpAmIL-4) produced mIL-4 at higher levels and was more stable in vitro than SL7207(pKKmIL-4). When SL7207(pOmpAmIL-A) was used as a live vaccine in BALB/c mice, this strain grew and survived at higher levels than the parental attenuated strain or empty plasmid-carrying strain in spleens, livers, and intestines. This difference in growth and survival did not appear to be caused by alterations in specific lymphocyte-mediated anti-Salmonella immune responses such as delayed-type hypersensitivity or serum antibody as measured by enzyme-linked immunosorbent assay; such alterations have been induced by IL-4 administration in other in vivo systems, and the lack of effect here may reflect the fact that IL-4 is not secreted from the bacteria in large quantities, most of the cytokine being in the cytoplasmic-membrane-bound fraction. Conversely, the ability of mouse macrophages to kill the bacteria in vitro was inhibited by bacterial production of mIL-4. This reduction in macrophage killing activity suggests that bacterial production of mIL-4 may be detrimental to host defense against Salmonella infection and may explain the enhanced bacterial growth and survival in vivo.

AN 1993:586004 BIOSIS

DN PREV199497005374

TI Expression of the murine interleukin-4 gene in an attenuated aroA strain

of Salmonella typhimurium: Persistence and immune response in BALB/c mice and susceptibility to macrophage killing.
AU **Denich, Kenneth (1)**; Borlin, Patrick; O'Hanley, Peter D.; Howard, Maureen; Heath, Andrew W.
CS (1) Dep. Med., Div. Infectious Diseases Geographic Med., Stanford Univ., Stanford, CA 94305-5402 USA
SO Infection and Immunity, (1993) Vol. 61, No. 11, pp. 4818-4827. ISSN: 0019-9567.
DT Article
LA English

L16 ANSWER 8 OF 11 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 2
AB The HlyA determinant among Escherichia coli isolates from patients with symptomatic urinary tract infection was compared in this report with a prototype HlyA encoded by pSF4000 by DNA-DNA hybridization tests with 20-base synthetic oligonucleotides and monoclonal antibody binding and neutralization assays. Hybridization results demonstrated that 349 (98%) of 357 definitive reactions among 54 hemolytic strains shared homology with seven DNA probes spanning many HlyA regions corresponding to residues (R) 41 to 47, 55 to 61, 248 to 254, 306 to 312, 336 to 343, 402 to 408, and 929 to 935. Genetic divergence was identified by lack of hybridization signals among 17 to 76% of the hemolytic strains within the distal portion of a predicted hydrophobic region corresponding to R491 to 319 and within a predicted hydrophilic region corresponding to R491 to 497 and R532 to 538. Serological studies demonstrated that 26 (81%) culture supernatants of 32 hemolytic strains were bound by all 12 monoclonal anti-HlyA antibodies. Among five of six remaining strains, the culture supernatants were bound by 3 to 11 monoclonal antibody preparations. There was only one hemolytic culture supernatant that failed to be bound by any monoclonal antibody, although the strain hybridized with nine hemolysin DNA probes. In addition, hemolytic activity of all 24 different culture supernatants tested was reduced by at least twofold by one monoclonal antibody specific for R2-161. These data extend and support previous views that the HlyA determinant is conserved among E. coli strains and suggest that a broadly cross-reactive HlyA subunit vaccine can be developed.
AN 1993:208554 BIOSIS
DN PREV199395109779
TI Genetic conservation of hlyA determinants and serological conservation of HlyA: Basis for developing a broadly cross-reactive subunit Escherichia coli alpha-hemolysin vaccine.
AU O'Hanley, Peter (1); Marcus, Rachel; Baek, Kwang Hyeon; **Denich, Kenneth**; Ji, Geun Eog
CS (1) Veterans Administration Hosp., Palo Alto, CA 94306 USA
SO Infection and Immunity, (1993) Vol. 61, No. 3, pp. 1091-1097. ISSN: 0019-9567.
DT Article
LA English

L16 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2002 ACS
AB Pyelonephritis-assocd. pili (Pap) are important in the pathogenesis of ascending, unobstructive E. coli-caused renal infections because these surface bacterial organelles mediate digalactoside-specific binding to host uroepithelial cells. Pap are composed of many different polypeptides, of which only the tip proteins mediate specific binding. The PapA moiety polymerizes to form the bulk of the pilus structure and has been employed in vaccines despite its lack of Gal.alpha.(1-4)Gal receptor specificity. Animal recipients of PapA pilus-based vaccines are protected against exptl. pyelonephritis caused by homologous and heterologous Gal-Gal-binding uropathogenic E. coli strains. Specific PapA IgG antibodies in urine are correlated with protection in these infection models. The nucleotide sequences of the gene encoding PapA were detd. for 3 E. coli clones expressing F71, F72, and F9 pili and were compared with corresponding sequences for other F serotypes. Specific rabbit antisera

were employed in ELISAs to study the cross-reactivity between Gal-Gal pili purified from recombinant strains expressing F71, F72, F9, or F13 pili and among 60 Gal-Gal-binding wild-type strains. Data are presented which corroborate the concept that papA genes are highly homologous and encode proteins which exhibit >70% homol. among pili of different serotypes. The differences primarily occur in the cysteine-cysteine loop and variable regions and constitute the basis for serol. diversity of these pili. Although there are differences in primary structures among these pili, antisera raised against pili of one serotype cross-reacted frequently with many other Gal-Gal pili of different serotypes. Furthermore, antisera raised against pili of the F13 serotype cross-reacted strongly or moderately with 52 (86%) of 60 wild-type Gal-Gal-binding E. coli strains. Thus, there are common immunogenic domains among these proteins. These addnl. data further support the hypothesis that broadly cross-protective PapA pilus vaccines for the immunoprophylaxis of pyelonephritis might be developed.

AN 1993:20542 CAPLUS
DN 118:20542
TI DNA sequences of three papA genes from uropathogenic Escherichia coli strains: evidence of structural and serological conservation
AU **Denich, Kenneth**; Blyn, Lawrence B.; Craiu, Abie; Braaten, Bruce A.; Hardy, Jonathan; Low, David A.; O'Hanley, Peter D.
CS Dep. Med., Stanford Univ., Stanford, CA, 94305, USA
SO Infection and Immunity (1991), 59(11), 3849-58
CODEN: INFIBR; ISSN: 0019-9567
DT Journal
LA English

L16 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2002 ACS
AB The frequency of selected papA DNA sequences among 89 digalactoside-binding, uropathogenic E. coli strains was evaluated with 12 different synthetic 15-base probes corresponding to papA genes from 4 digalactoside-binding piliated recombinant strains (HU849, 201B, 210B, and 200A). The papA probes encode amino acids which are common at the carboxy terminus of all strains, adjacent to the proximal portion of the intramol. disulfide loop of strain 210B, or predicted to constitute the type-specific epitope for each of the 4 recombinant strains or other epitopes of strain HU849. The presence among the strains of DNA sequence homol. to the papA probes was detd. by in situ colony hybridization. Hybridization data suggest that gene from strain HU849 among the clin. strains. The following nucleotide locations which encode portions of the mature HU849 PapA are detected in a high percentage (42 to 70%) of clin. isolates: 208 to 222, 310 to 324, 478 to 492, 517 to 531, 553 to 567, and 679 to 693. These sequences encode portions of the predicted protective, immunogenic, and/or antigenic epitopes of this PapA. The data also indicate considerable heterogeneity of papA sequences among the strains, esp. in the region of nucleotide bases corresponding to positions 391 to 418. These oligonucleotides encode the predicted PapA type-specific immunogenic dominant epitope. Detn. of the extent of genetic variability in the papA gene among digalactoside-binding strains will require more extensive DNA sequencing of prototypic papA genes, addnl. hybridization studies employing other papA gene oligonucleotide probes, the assessment of the different pap operons and their copy no. in each strain.

AN 1991:671733 CAPLUS
DN 115:271733
TI Frequency and organization of papA homologous DNA sequences among uropathogenic digalactoside-binding Escherichia coli strains
AU **Denich, Kenneth**; Craiu, Abie; Rugo, Hope; Muralidhar, Girija; O'Hanley, Peter
CS Dep. Med., Stanford Univ., Stanford, CA, 94305, USA
SO Infection and Immunity (1991), 59(6), 2089-96
CODEN: INFIBR; ISSN: 0019-9567
DT Journal
LA English

L16 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2002 ACS

AB Thirty-six recessive temp.-sensitive (ts) mutants in 30 sep. emb genes, which cause arrest of embryonic development, were isolated in the nematode C. elegans. Twenty-five emb genes were mapped; 10 of them were clustered near gene unc-32 on linkage group III. Characterization of these ts mutants genetically and phenotypically aided in elucidation of the role of maternal and zygotic gene expression in each of the developmental steps visible at the cellular level.

AN 1982:140094 CAPLUS

DN 96:140094

TI Genetic dissection of embryogenesis in Caenorhabditis elegans

AU Cassada, Randall; Isnenghi, Edoardo; **Denich, Kenneth**; Radnia, Khosro; Schierenberg, Einhard; Smith, Kenneth; Von Ehrenstein, Guenter

CS Dep. Mol. Biol., Max-Planck-Inst. Exp. Med., Goettingen, D-3400, Fed. Rep. Ger.

SO ICN-UCLA Symp. Mol. Cell. Biol. (1981), 23, 209-27
CODEN: IUSMDJ; ISSN: 0097-9023

DT Journal

LA English

=> FIL STNGUIDE

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FULL ESTIMATED COST	231.09	231.30

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FILE 'STNGUIDE' ENTERED AT 16:19:37 ON 09 OCT 2002

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Oct 4, 2002 (20021004/UP).

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7 ANSWER 1 OF 18 USPATFULL
AB A method of producing **pili** and vaccines containing **pili** are described using bacteria that express at least one immunogenic peptide in a PapA region that does not normally contain such a peptide.
AN 2002:258441 USPATFULL
TI Immunogenic **pili** presenting foreign peptides, their production and use
IN O'Hanley, Peter, Washington, DC, UNITED STATES
Denich, Kenneth, Edmonton, CANADA
Schmidt, M. Alexander, Muenster, GERMANY, FEDERAL REPUBLIC OF
PI US 2002142008 A1 20021003
AI US 2001-833079 A1 20010412 (9)
PRAI US 2000-196491P 20000412 (60)
DT Utility
FS APPLICATION
LREP FOLEY AND LARDNER, SUITE 500, 3000 K STREET NW, WASHINGTON, DC, 20007
CLMN Number of Claims: 7
ECL Exemplary Claim: 1
DRWN 5 Drawing Page(s)
LN.CNT 967

L7 ANSWER 2 OF 18 USPATFULL
AB A strategically modified hepatitis B core protein is described, where an insert is provided, preferably in an immunodominant region of the nucleocapsid protein, containing a chemically reactive amino acid residue. The modified hepatitis B core protein or its aggregated nucleocapsid protein particles can be pendently linked to a hapten to form a modified nucleocapsid conjugate. Such a conjugate is useful in the preparation of vaccines or antibodies. The modified hepatitis B core protein can also be modified to include a T cell epitope.
AN 2001:71101 USPATFULL
TI Strategically modified hepatitis B core proteins and their derivatives
IN Birkett, Ashley J., Solana Beach, CA, United States
PA Immune Complex Corporation, San Diego, CA, United States (U.S. corporation)
PI US 6231864 B1 20010515
AI US 1999-248588 19990211 (9)
PRAI US 1998-74537P 19980212 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: Wortman, Donna C.
LREP Welsh & Katz, Ltd.
CLMN Number of Claims: 22
ECL Exemplary Claim: 1
DRWN 1 Drawing Figure(s); 1 Drawing Page(s)
LN.CNT 1665
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 3 OF 18 USPATFULL
AB The present invention is directed to recombinant genes and their encoded proteins which are recombinant flagellin fusion proteins. Such fusion proteins comprise amino acid sequences specifying an epitope encoded by a flagellin structural gene and an epitope of a heterologous organism which is immunogenic upon introduction of the fusion protein into a vertebrate host. The recombinant genes and proteins of the present invention can be used in vaccine formulations, to provide protection against infection by the heterologous organism, or to provide protection against conditions or disorders caused by an antigen of the organism. In a specific embodiment, attenuated invasive bacteria expressing the recombinant flagellin genes of the invention can be used in live vaccine formulations. The invention is illustrated by way of examples in which epitopes of malaria circumsporozoite antigens, the B subunit of Cholera toxin, surface and presurface antigens of Hepatitis B. VP7 polypeptide

of rotavirus, envelope glycoprotein of HIV, and M protein of Streptococcus, are expressed in recombinant flagellin fusion proteins which assemble into functional flagella, and which provoke an immune response directed against the heterologous epitope, in a vertebrate host.

AN 2000:134749 USPATFULL
TI Recombinant flagellin vaccines
IN Majarian, William R., Mt. Royal, NJ, United States
Stocker, Bruce A. D., Palo Alto, CA, United States
Newton, Salete M. C., Mountain View, CA, United States
PA American Cyanamid Company, Madison, NJ, United States (U.S. corporation)
The Board of Trustees of the Leland Stanford Junior University, Stanford, CA, United States (U.S. corporation)
PI US 6130082 20001010
AI US 1992-837668 19920214 (7)
RLI Continuation of Ser. No. US 1989-348430, filed on 5 May 1989, now abandoned which is a continuation-in-part of Ser. No. US 1988-190570, filed on 5 May 1988, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Mosher, Mary E.
LREP Hamilton, Brook, Smith & Reynolds, P.C.
CLMN Number of Claims: 3
ECL Exemplary Claim: 1
DRWN 15 Drawing Figure(s); 17 Drawing Page(s)
LN.CNT 2404
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 4 OF 18 USPATFULL
AB A CS31A protein capsule subunit having an aminoacid sequence modified by at least one heterologous peptide, the CS31A protein capsule comprising said subunit, and micro-organisms having the CS31A protein capsule with its subunit aminoacid sequence modified by at least one heterologous peptide, are disclosed. Methods for preparing said subunits, CS31A protein capsules comprising same, and micro-organisms having CS31A protein capsules, as well as the use thereof for preparing vaccines, producing peptides and preparing immunoassays, are also disclosed.

AN 2000:98007 USPATFULL
TI ClpG subunit of CS31A protein capsule containing heterologous peptides
IN Girardeau, Jean-Pierre, Saint Genes Champanelle, France
Martin, Christine, La Roche Blanche, France
Mechin, Marie-Claire, Beaumont, France
Der Vartanian, Maurice, Saint Genes Champanelle, France
Bousquet, Fran.cedilla.ois, Ceyrat, France
PA Institut National de la Recherche Agronomique-INRA, Paris, France (non-U.S. corporation)
PI US 6096321 20000801
WO 9414967 19940707
AI US 1996-491954 19960216 (8)
WO 1993-FR1281 19931221
19960216 PCT 371 date
19960216 PCT 102(e) date
PRAI FR 1992-15464 19921222
DT Utility
FS Granted
EXNAM Primary Examiner: Chin, Christopher L.; Assistant Examiner: Ryan, V.
LREP Schnader Harrison Segal & Lewis LLP
CLMN Number of Claims: 29
ECL Exemplary Claim: 1
DRWN 61 Drawing Figure(s); 53 Drawing Page(s)
LN.CNT 3468
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 5 OF 18 USPATFULL

AB The present invention is concerned with vaccination of mammals against GnRH. The vaccine comprises a GnRH peptide conjugate to E. coli fimbrial-filaments and elicits an immune response against GnRH.
AN 2000:12446 USPATFULL
TI Carrier system against GnRH
IN Van Der Zee, Anna, Woerden, Netherlands
Van Die, Irma Marianne, Gouda, Netherlands
Hoekstra, Willem Pieter Martin, Zeist, Netherlands
Gielen, Josephus Theodorus, St. Antohonis, Netherlands
PA Akzo Nobel N.V., Arnhem, Netherlands (non-U.S. corporation)
PI US 6019983 20000201
AI US 1995-521079 19950829 (8)
RLI Continuation of Ser. No. US 1993-78661, filed on 16 Jun 1993, now abandoned
PRAI NL 1982-92201775 19820619
DT Utility
FS Granted
EXNAM Primary Examiner: Sidberry, Hazel F.
LREP Gormley, Mary E., Blackstone, William M.
CLMN Number of Claims: 6
ECL Exemplary Claim: 1
DRWN 9 Drawing Figure(s); 9 Drawing Page(s)
LN.CNT 1366
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 6 OF 18 LIFESCI COPYRIGHT 2002 CSA
AB Recombinant live oral vaccines expressing pathogen-derived antigens offer a unique set of attractive properties. Among these are the simplicity of administration, the capacity to induce mucosal and systemic immunity, and the advantage of permitting genetic manipulation for optimal antigen presentation. In this study, the benefit of having a heterologous antigen expressed on the surface of a live vector rather than intracellularly was evaluated. Accordingly, the immune response of mice immunized with a Salmonella enterica serovar Typhimurium vaccine strain expressing the Escherichia coli 987P fimbrial antigen on its surface (Fas super(+)) was compared with the expression in the periplasmic compartment (Fas super(-)). Orally immunized BALB/c mice showed that 987P fimbriated Salmonella serovar Typhimurium CS3263 (aroA asd) with pCS151 (fas super(+) asd super(+)) elicited a significantly higher level of 987P-specific systemic immunoglobulin G (IgG) and mucosal IgA than serovar Typhimurium CS3263 with pCS152 (fasD mutant, asd super(+)) expressing 987P periplasmic antigen. Further studies were aimed at determining whether the 987P fimbriae expressed by serovar Typhimurium chi 4550 (cya crp asd) could be used as carriers of **foreign epitopes**. For this, the vaccine strain was genetically engineered to express chimeric fimbriae carrying the transmissible gastroenteritis virus (TGEV) C (379-388) and A (521-531) epitopes of the spike protein inserted into the 987P major fimbrial subunit FasA. BALB/c mice administered orally serovar Typhimurium chi 4550 expressing the chimeric fimbriae from the tet promoter in pCS154 (fas super(+) asd super(+)) produced systemic antibodies against both fimbria and the TGEV C epitope but not against the TGEV A epitope. To improve the immunogenicity of the chimeric fimbriae, the in vivo inducible nirB promoter was inserted into pCS154, upstream of the fas genes, to create pCS155. In comparison with the previously used vaccine, BALB/c mice immunized orally with serovar Typhimurium chi 4550/pCS155 demonstrated significantly higher levels of serum IgG and mucosal IgA against 987P fimbria. Moreover, mucosal IgA against the TGEV C epitope was only detected with serovar Typhimurium chi 4550/pCS155. The induced antibodies also recognized the epitopes in the context of the full-length TGEV spike protein. Hence, immune responses to heterologous chimeric fimbriae on Salmonella vaccine vectors can be optimized by using promoters known to be activated in vivo.
AN 2000:88925 LIFESCI
TI Mucosal and systemic immune responses to chimeric fimbriae expressed by

Salmonella enterica serovar Typhimurium vaccine strains
AU Chen, H.; Schifferli, D.M.*
CS University of Pennsylvania School of Veterinary Medicine, 3800 Spruce St., Philadelphia, PA 19104-6049, USA; E-mail: dmschiff@vet.upenn.edu
SO Infection and Immunity [Infect. Immun.], (20000600) vol. 68, no. 6, pp. 3129-3139.
ISSN: 0019-9567.
DT Journal
FS J; F
LA English
SL English

L7 ANSWER 7 OF 18 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 1
AB Objective: To construct the display vector based on the CS3 **pili** of enterotoxigenic Escherichia coli. Methods: The secondary structure antigen epitopes, hydrophilicity and flexibility of CS3 subunit were predicted with the Goldkey software. Based on the prediction, the site for inserting heterologous epitopes was chosen. Mutation was done using the overlapping extention PCR. The gene fragment coding for the VP1 of foot-mouth disease virus (FMDV) was synthesized and inserted into CS3. The surface expression of hybrid protein was examined using whole-cell ELISA, electron microscopy and immuno-electron microscopy. Mice were immunized by injecting the recombinant bacteria intraperitoneally to evaluate the immunogenicity of the hybrid proteins. Results: The VP1 of FMDV was displayed on the surface of the recombinant cells. The fusion proteins were expressed as hybrid **pili**. Mice produced antibody response against CS3 and the VP1 of FMDV. Conclusion: The CS3 **pili** can be a vector to express the **foreign epitopes** on the surface of the recombinant cells, and it may probably be an expression vector for the construction of the live gene engineering vaccine.
AN 2001:49887 BIOSIS
DN PREV200100049887
TI Construction of a display vector based on the CS3 **pili** of enterotoxigenic Escherichia coli.
AU Gao Rongkai; Zhang Zhaoshan (1); Li Shuqin
CS (1) Academy of Military Medical Science, Institute of Biotechnology, Beijing, 100071: zhangzs@nic.bmi.ac.cn China
SO Zhonghua Weishengwuxue He Mianyixue Zazhi, (November, 2000) Vol. 20, No. 6, pp. 485-488. print.
ISSN: 0254-5101.
DT Article
LA Chinese
SL Chinese; English

L7 ANSWER 8 OF 18 LIFESCI COPYRIGHT 2002 CSA
AB The strong immunogenicity of bacterial fimbriae results from their polymeric and proteinaceous nature, and the protective role of these immunogens in experimental or commercial vaccines is associated with their capacity to induce antiadhesive antibodies. Fimbria-mediated intestinal colonization by enteropathogens typically leads to similar antibody responses. The possibility of taking advantage of these properties was investigated by determining whether enteroadhesive fimbriae, like the 987P fimbriae of enterotoxigenic Escherichia coli, can serve as carriers for foreign antigens without losing their adhesive characteristics. Random linker insertion mutagenesis of the fasA gene encoding the major 987P subunit identified five different mutants expressing wild-type levels of fimbriation. The linker insertion sites of these mutants were used to introduce three continuous segments of viral surface glycoproteins known to be accessible to antibodies. These segments encode residues 11 to 19 or 272 to 279 of herpes simplex virus type 1 (HSV-1) glycoprotein D [gD(11-19) and gD(272-279), respectively] or residues 379 to 388 of the transmissible gastroenteritis virus (TGEV) spike protein [S(379-388)]. Studies of bacteria expressing fimbriae incorporating mutated FasA

subunits alone or together with wild-type FasA subunits (hybrid fimbriae) indicated that **foreign epitopes** were best exported and displayed on assembled fimbriae when they were inserted near the amino terminus of FasA. Fimbriated bacteria expressing FasA subunits carrying the HSV gD(11-19) or the TGEV S(379-388) epitope inserted between the second and third residues of mature FasA elicited high levels of foreign epitope antibodies in all rabbits immunized parenterally. Antibodies against the HSV epitope were also shown to recognize the epitope in the context of the whole gD protein. Because the 987P adhesive subunit FasG was shown to be present on mutated fimbriae and to mediate bacterial attachment to porcine intestinal receptors, polymeric display of **foreign epitopes** on 987P offers new opportunities to test the potential beneficial effect of enteroadhesion for mucosal immunization and protection against various enteric pathogens.

AN 1999:42426 LIFESCI
TI Polymeric Display of Immunogenic Epitopes from Herpes Simplex Virus and Transmissible Gastroenteritis Virus Surface Proteins on an Enteroadherent Fimbria
AU Rani, D.B.R.; Bayer, M.E.; Schifferli, D.M.*
CS University of Pennsylvania School of Veterinary Medicine, 3800 Spruce St., Philadelphia, PA 19104-6049, USA; E-mail: dmschiff@vet.upenn.edu
SO Clinical and Diagnostic Laboratory Immunology [Clin. Diagn. Lab. Immunol.], (19990100) vol. 6, no. 1, pp. 30-40. ISSN: 1071-412X.
DT Journal
FS V; F
LA English
SL English

L7 ANSWER 9 OF 18 USPATFULL
AB In order to obtain a novel binding protein against a chosen target, DNA molecules, each encoding a protein comprising one of a family of similar potential binding domains and a structural signal calling for the display of the protein on the outer surface of a chosen bacterial cell, bacterial spore or phage (genetic package) are introduced into a genetic package. The protein is expressed and the potential binding domain is displayed on the outer surface of the package. The cells or viruses bearing the binding domains which recognize the target molecule are isolated and amplified. The successful binding domains are then characterized. One or more of these successful binding domains is used as a model for the design of a new family of potential binding domains, and the process is repeated until a novel binding domain having a desired affinity for the target molecule is obtained. In one embodiment, the first family of potential binding domains is related to bovine pancreatic trypsin inhibitor, the genetic package is M13 phage, and the protein includes the outer surface transport signal of the M13 gene III protein.

AN 1998:143904 USPATFULL
TI Directed evolution of novel binding proteins
IN Ladner, Robert Charles, Ijamsville, MD, United States
Gutterman, Sonia Kosow, Belmont, MA, United States
Roberts, Bruce Lindsay, Milford, MA, United States
Markland, William, Milford, MA, United States
Ley, Arthur Charles, Newton, MA, United States
Kent, Rachel Baribault, Boxborough, MA, United States
PA Dyax, Corp., Cambridge, MA, United States (U.S. corporation)
PI US 5837500 19981117
AI US 1995-415922 19950403 (8)
RLI Continuation of Ser. No. US 1993-9319, filed on 26 Jan 1993, now patented, Pat. No. US 5403484 which is a division of Ser. No. US 1991-664989, filed on 1 Mar 1991, now patented, Pat. No. US 5223409 which is a continuation-in-part of Ser. No. US 1990-487063, filed on 2 Mar 1990, now abandoned which is a continuation-in-part of Ser. No. US 1988-240160, filed on 2 Sep 1988, now abandoned

DT Utility
FS Granted
EXNAM Primary Examiner: Ulm, John
LREP Cooper, Iver P.
CLMN Number of Claims: 43
ECL Exemplary Claim: 1
DRWN 16 Drawing Figure(s); 16 Drawing Page(s)
LN.CNT 15973
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 10 OF 18 CAPLUS COPYRIGHT 2002 ACS
AB To develop a system which allows infection by an epitope-specific phage-antibody via an F-pilus expressing that epitope, a study on the expression of foreign sequences on F-pilin was undertaken. Initially, a plasmid library was constructed with random sequences encoding one to five amino acid residues fused to the C terminus of F-pilin (traA) which was used to complement an F-plasmid with an amber mutation in traA. Functional F-pilin fusions were detected using the filamentous phage, fUSE2, which transduces tetracycline resistance, as well as immunoblots using a monoclonal antiserum specific for the acetylated N terminus of pilin. All the clones selected expressed the pilin-fusions and displayed full sensitivity towards fUSE2 infection, which was indistinguishable from the wild-type F-pilin. The sequences of fUSE2-sensitive clones when compared to randomly selected clones which were not fUSE2-sensitive, revealed no obvious pattern in the amino acid residues fused to the C terminus, except for a preference for a hydrophilic amino acid at position +1. Mutating the C-terminal Leu in wt (wild-type) pilin to Ser blocked pilus assembly and fUSE2 infection; the pilin was correctly processed but the level of acetylation at the N terminus appeared to decrease. Fusing a known epitope (myc) directly to the C terminus blocked processing of F-pilin leading to loss of F-pilus assembly and function. The introduction of random sequences between traA and this epitope yielded fully recombinant, functional F-**pili** but this appeared to be due to processing of the extension by an unidentified protease,leading to loss of the epitope. Surface expression of another epitope (G2-10) was clearly demonstrated by immuno-electron microscopy of **pili** with a G2-10 monoclonal antibody. A different five amino acid residue spacer between the F-pilin C terminus and the G2-10 epitope produced a system that was transfer-proficient and fUSE2-sensitive, but the **pili** were barely detectable by immunoblots or by electron microscopy. While the underlying rules that govern successful epitope expression at the C terminus of F-pilin remain elusive, many types of foreign sequences can be displayed with varying degrees of success. The authors' results also suggest that pilin sequence dets. a no. of steps in the complex pathway for pilus assembly.
AN 1998:408570 CAPLUS
DN 129:172576
TI Epitopes fused to F-pilin are incorporated into functional recombinant **pili**
AU Rondot, S.; Anthony, K. G.; Diubel, S.; Ida, N.; Wiemann, S.; Beyreuther, K.; Frost, L. S.; Little, M.; Breitling, F.
CS German Cancer Research Center, Heidelberg, Germany
SO Journal of Molecular Biology (1998), 279(3), 589-603
CODEN: JMOBAK; ISSN: 0022-2836
PB Academic Press Ltd.
DT Journal
LA English

L7 ANSWER 11 OF 18 USPATFULL
AB The present invention is concerned with vaccination of mammals against GnRH. The vaccine comprises a GnRH peptide conjugate to E. coli fimbrial-filaments and elicits an immune response against GnRH.
AN 97:101896 USPATFULL
TI Carrier system against GNRH

IN Van Der Zee, Anna, Woerden, Netherlands
Van Die, Irma Marianne, Gouda, Netherlands
Hoekstra, Willem Pieter Martin, Zeist, Netherlands
Gielen, Josephus Theodorus, St. Antohonis, Netherlands
PA AKZO Nobel N.V., Arnhem, Netherlands (non-U.S. corporation)
PI US 5684145 19971104
AI US 1995-453588 19950530 (8)
RLI Division of Ser. No. US 1993-78661, filed on 16 Jun 1993, now abandoned
PRAI NL 1992-1775 19920618
DT Utility
FS Granted
EXNAM Primary Examiner: Sidberry, Hazel F.
LREP Gormley, Mary E.
CLMN Number of Claims: 8
ECL Exemplary Claim: 1
DRWN 9 Drawing Figure(s); 9 Drawing Page(s)
LN.CNT 1299
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 12 OF 18 USPATFULL
AB In order to obtain a novel binding protein against a chosen target, DNA molecules, each encoding a protein comprising one of a family of similar potential binding domains and a structural signal calling for the display of the protein on the outer surface of a chosen bacterial cell, bacterial spore or phage (genetic package) are introduced into a genetic package. The protein is expressed and the potential binding domain is displayed on the outer surface of the package. The cells or viruses bearing the binding domains which recognize the target molecule are isolated and amplified. The successful binding domains are then characterized. One or more of these successful binding domains is used as a model for the design of a new family of potential binding domains, and the process is repeated until a novel binding domain having a desired affinity for the target molecule is obtained. In one embodiment, the first family of potential binding domains is related to bovine pancreatic trypsin inhibitor, the genetic package is M13 phage, and the protein includes the outer surface transport signal of the M13 gene III protein.
AN 96:101466 USPATFULL
TI Directed evolution of novel binding proteins
IN Ladner, Robert C., Ijamsville, MD, United States
Guterman, Sonia K., Belmont, MA, United States
Roberts, Bruce L., Milford, MA, United States
Markland, William, Milford, MA, United States
Ley, Arthur C., Newton, MA, United States
Kent, Rachel B., Boxborough, MA, United States
PA Protein Engineering Corporation, Cambridge, MA, United States (U.S. corporation)
PI US 5571698 19961105
AI US 1993-57667 19930618 (8)
DCD 20100629
RLI Continuation of Ser. No. US 1991-664989, filed on 1 Mar 1991, now patented, Pat. No. US 5223409 which is a continuation-in-part of Ser. No. US 1990-487063, filed on 2 Mar 1990, now abandoned which is a continuation-in-part of Ser. No. US 1988-240160, filed on 2 Sep 1988, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Ulm, John
LREP Cooper, Iver P.
CLMN Number of Claims: 83
ECL Exemplary Claim: 1
DRWN 16 Drawing Figure(s); 16 Drawing Page(s)
LN.CNT 15323
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 13 OF 18 USPATFULL

AB In order to obtain a novel binding protein against a chosen target, DNA molecules, each encoding a protein comprising one of a family of similar potential binding domains and a structural signal calling for the display of the protein on the outer surface of a chosen bacterial cell, bacterial spore or phage (genetic package) are introduced into a genetic package. The protein is expressed and the potential binding domain is displayed on the outer surface of the package. The cells or viruses bearing the binding domains which recognize the target molecule are isolated and amplified. The successful binding domains are then characterized. One or more of these successful binding domains is used as a model for the design of a new family of potential binding domains, and the process is repeated until a novel binding domain having a desired affinity for the target molecule is obtained. In one embodiment, the first family of potential binding domains is related to bovine pancreatic trypsin inhibitor, the genetic package is M13 phage, and the protein includes the outer surface transport signal of the M13 gene III protein.

AN 95:29292 USPATFULL

TI Viruses expressing chimeric binding proteins

IN Ladner, Robert C., Ijamsville, MD, United States
Guterman, Sonia K., Belmont, MA, United States
Roberts, Bruce L., Milford, MA, United States
Markland, William, Milford, MA, United States
Ley, Arthur C., Newton, MA, United States
Kent, Rachel B., Boxborough, MA, United States

PA Protein Engineering Corporation, Cambridge, MA, United States (U.S. corporation)

PI US 5403484 19950404

AI US 1993-9319 19930126 (8)

RLI Division of Ser. No. US 1991-664989, filed on 1 Mar 1991, now patented, Pat. No. US 5223409 which is a continuation-in-part of Ser. No. US 1990-487063, filed on 2 Mar 1990, now abandoned which is a continuation-in-part of Ser. No. US 1988-240160, filed on 2 Sep 1988, now abandoned

PRAI WO 1989-3731 19890901

DT Utility

FS Granted

EXNAM Primary Examiner: Hill, Jr., Robert J.; Assistant Examiner: Ulm, John D.

LREP Cooper, Iver P.

CLMN Number of Claims: 49

ECL Exemplary Claim: 1

DRWN 16 Drawing Figure(s); 16 Drawing Page(s)

LN.CNT 14368

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 14 OF 18 USPATFULL

AB In order to obtain a novel binding protein against a chosen target, DNA molecules, each encoding a protein comprising one of a family of similar potential binding domains and a structural signal calling for the display of the protein on the outer surface of a chosen bacterial cell, bacterial spore or phage (genetic package) are introduced into a genetic package. The protein is expressed and the potential binding domain is displayed on the outer surface of the package. The cells or viruses bearing the binding domains which recognize the target molecule are isolated and amplified. The successful binding domains are then characterized. One or more of these successful binding domains is used as a model for the design of a new family of potential binding domains, and the process is repeated until a novel binding domain having a desired affinity for the target molecule is obtained. In one embodiment, the first family of potential binding domains is related to bovine pancreatic trypsin inhibitor, the genetic package is M13 phage, and the protein includes the outer surface transport signal of the M13 gene III

protein.
AN 93:52487 USPATFULL
TI Directed evolution of novel binding proteins
IN Ladner, Robert C., Ijamsville, MD, United States
Guterman, Sonia K., Belmont, MA, United States
Roberts, Bruce L., Milford, MA, United States
Markland, William, Milford, MA, United States
Ley, Arthur C., Newton, MA, United States
Kent, Rachel B., Boxborough, MA, United States
PA Protein Engineering Corp., Cambridge, MA, United States (U.S. corporation)
PI US 5223409 19930629
AI US 1991-664989 19910301 (7)
RLI Continuation-in-part of Ser. No. US 1990-487063, filed on 2 Mar 1990, now abandoned And a continuation-in-part of Ser. No. US 1988-240160, filed on 2 Sep 1988, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Hill, Jr., Robert J.; Assistant Examiner: Ulm, John D.
LREP Cooper, Iver P.
CLMN Number of Claims: 66
ECL Exemplary Claim: 1
DRWN 16 Drawing Figure(s); 16 Drawing Page(s)
LN.CNT 15410
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 15 OF 18 USPATFULL
AB The present invention relates to recombinant vector/host systems which can direct the expression of foreign genes under the control of the Heliothis polyhedrin promoter. Using the systems of the present invention, a heterologous gene of interest can be expressed as an unfused peptide or protein, a fusion protein, or as a recombinant occlusion body which comprises crystallized polyhedrin fusion proteins bearing the heterologous gene product on the surface of or within the occlusion body. The recombinant proteins or occlusion bodies of the present invention have uses in vaccine formulations and immunoassays, as biological insecticides, and as expression systems for the production of foreign peptides or proteins.
AN 91:66733 USPATFULL
TI Heliothis expression systems
IN Fraser, Malcolm J., South Bend, IN, United States
Rosen, Elliot D., South Bend, IN, United States
Ploplis, Victoria A., South Bend, IN, United States
PA American Biogenetic Science, Inc., Copiague, NY, United States (U.S. corporation)
PI US 5041379 19910820
AI US 1988-168109 19880314 (7)
RLI Continuation-in-part of Ser. No. US 1987-26499, filed on 16 Mar 1987, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Schwartz, Richard A.; Assistant Examiner: Peet, Richard C.
LREP Pennie & Edmonds
CLMN Number of Claims: 15
ECL Exemplary Claim: 1
DRWN 26 Drawing Figure(s); 25 Drawing Page(s)
LN.CNT 3494
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 16 OF 18 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 2
AB The K88 fimbriae of enterotoxigenic Escherichia coli are strongly immunogenic antigens that can be used to evoke protective immunity. To find out whether these fimbriae can be used as carriers for

foreign epitopes, a highly variable region present in the primary structure of the different K88 variants was replaced with five different heterologous epitopes to investigate to what extent these insertions affected the expression, assembly (biogenesis), stability and immunogenic properties of the resulting hybrid fimbriae. Amino acid residues 163-173, were replaced using site-directed in vitro mutagenesis and the hybrid fimbriae were tested for these aspects using ELISA, immunoelectronmicroscopy and immunoblotting. Replacement of this highly variable region did not affect the biosynthesis of fimbriae, although all mutations tested resulted in a reduced expression depending on the epitope inserted. Testing of the different hybrid fimbriae with a panel of monoclonal antibodies raised against the various K88 serotypes K88ab, K88ac and K88ad indicated that replacement of amino acid sequence 163-173 did not affect conserved or K88ab specific epitopes but the K88ac and K88ad specific conformation was lost. Immunization with hybrid fimbriae raises antibodies specific for the inserted heterologous epitopes.

AN 1991:40562 CAPLUS
DN 114:40562
TI K88 fimbriae as carriers of heterologous antigenic determinants
AU Bakker, D.; Van Zijderveld, F. G.; Van der Veen, S.; Oudega, B.; De Graaf, F. K.
CS Fac. Biol., Vrije Univ., Amsterdam, Neth.
SO Microbial Pathogenesis (1990), 8(5), 343-52
CODEN: MIPAEV; ISSN: 0882-4010
DT Journal
LA English

L7 ANSWER 17 OF 18 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 3
AB Hypervariable regions (HRs) of the major subunit of F11 fimbriae were exploited for insertion of **foreign epitopes**. Two insertion vectors were created that contain a unique cloning site in HR1 or HR4, resp. Several oligonucleotides, coding for antigenic determinants derived from different pathogens, were cloned in both insertion vectors. Hybrid fimbrial subunits were generally shown to be assembled in fimbriae when the length of the inserted peptide did not exceed 14 amino acids. The inserted peptides appeared to be exposed in the fimbrial filament. One hybrid fimbrial protein induced detectable levels of antibodies against the inserted epitope if injected into mice.

AN 1990:527644 CAPLUS
DN 113:127644
TI Expression of **foreign epitopes** in P-fimbriae of Escherichia coli
AU Van Die, Irma; Van Oosterhout, Joost; Van Megen, Ingrid; Bergmans, Hans; Hoekstra, Wiel; Enger-Valk, Betty; Barteling, Simon; Mooi, Frits
CS Dep. Mol. Cell Biol., Univ. Utrecht, Utrecht, 3584 CH, Neth.
SO MGG, Mol. Gen. Genet. (1990), 222(2-3), 297-303
CODEN: MGGEAE; ISSN: 0026-8925
DT Journal
LA English

L7 ANSWER 18 OF 18 USPATFULL
AB The present invention is directed to recombinant baculoviruses which encode fusion polyhedrin proteins capable of forming occlusion bodies containing foreign peptides. The recombinant baculoviruses of the invention are formed by insertion into or replacement of regions of the polyhedrin gene that are not essential for occlusion body formation, with foreign DNA fragments by recombinant DNA techniques. The recombinant occlusion bodies produced in accordance with the present invention have uses in vaccine formulations, immunoassays, immobilized enzyme reactions, as biological insecticides, and as expression vectors.

AN 89:80739 USPATFULL
TI Recombinant baculovirus occlusion bodies in vaccines and biological insecticides
IN Fraser, Malcolm J., South Bend, IN, United States

Rosen, Elliot D., South Bend, IN, United States
Ploplis, Victoria A., South Bend, IN, United States
PA American Biogenetic Sciences, Inc., Copiague, NY, United States (U.S. corporation)
PI US 4870023 19890926
AI US 1988-153736 19880208 (7)
RLI Continuation-in-part of Ser. No. US 1987-26498, filed on 16 Mar 1987, now abandoned which is a continuation-in-part of Ser. No. US 1987-26499, filed on 16 Mar 1987
DT Utility
FS Granted
EXNAM Primary Examiner: Wiseman, Thomas G.; Assistant Examiner: Seidman, Stephanie
LREP Pennie & Edmonds
CLMN Number of Claims: 51
ECL Exemplary Claim: 1
DRWN 28 Drawing Figure(s); 26 Drawing Page(s)
LN.CNT 3868
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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09/833,091

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show files
File 155:MEDLINE(R) 1966-2002/Jul W1
File   5:Biosis Previews(R) 1969-2002/Jul W1
         (c) 2002 BIOSIS
File 315:ChemEng & Biotec Abs 1970-2001/Dec
         (c) 2002 DECHEMA
File  73:EMBASE 1974-2002/Jul W1
         (c) 2002 Elsevier Science B.V.
File 399:CA SEARCH(R) 1967-2002/UD=13627
         (c) 2002 AMERICAN CHEMICAL SOCIETY
File 351:Derwent WPI 1963-2002/UD,UM &UP=200243
         (c) 2002  Thomson Derwent
?ds

Set     Items   Description
S1        284   GAL()GAL
S2      11113   PILI OR PILUS
S3        811   PAPA
S4        256   PAP()A
S5    2991115   BACTERI?
S6      70963   UTI OR (URINARY(5N)TRACT(5N)INFECTION? ?)
S7     342815   VACCINE? ? OR VACCINAT?
S8    1874913   DETACH? OR RELEASE? ? OR DISSOCIAT?
S9   11893872   TREAT? OR PREVENT? OR THERAP?
S10    869214   INSERT?
S11    573343   FUSION OR FUSED OR CHIMER? OR CHIMAER?
S12   5830731   PEPTIDE? ? OR POLYPEPTIDE? ? OR PROTEIN? ?
S13     97163   HETEROLOG?
S14    127160   FOREIGN
S15        44   AU=DENICH K? OR AU=DENICH, K?
S16       269   E11-E19 OR E24-E28
S17      2925   E3-E6
S18       871   E4-E8
S19      4074   S15-S18
S20       796   S3 NOT (PAPA(3N)SYNDROME? ?)
S21        32   S19 AND S1
S22       193   DIGALACTOSIDE? ?
S23        20   S19 AND S22
S24        33   (S21 OR S23) AND S2
S25        14   RD S24 (unique items)
S26        59   (S1 OR S22) (5N) S2
S27        81   (S1 OR S22) AND S2
S28        25   S27 AND (S3 OR S4)
S29        16   RD S28 (unique items)
S30        27   S27 AND (S10 OR S11 OR S13 OR S14)
S31        13   RD S30 (unique items)
S32        31   S25 OR S29 OR S31
S33    172279   (S10 OR S11 OR S13 OR S14) (5N) S12
S34        43   S2 (5N) S33
S35         4   S34 AND (S3 OR S4)
S36         3   RD S35 (unique items)
S37        33   S32 OR S36
S38       166   S6 (5N) S7
S39        24   S38 AND S2
S40        22   RD S39 (unique items)
S41         2   S40 AND (S3 OR S4)
S42         2   RD S41 (unique items)
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S43 33 S37 OR S42
S44 19 S40 NOT S43
S45 2 S44 AND (S1 OR S22)
S46 35 S45 OR S43
S47 34 RD S46 (unique items)
?t 47/7/all

47/7/1 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07105311 92040048 PMID: 1682251

DNA sequences of three papA genes from uropathogenic Escherichia coli strains: evidence of structural and serological conservation.

Denich K ; Blyn L B; Craiu A; Braaten B A; Hardy J; Low D A; O'Hanley P D

Department of Medicine, Stanford University, California 94305.

Infection and immunity (UNITED STATES) Nov 1991, 59 (11) p3849-58, ISSN 0019-9567 Journal Code: 0246127

Contract/Grant No.: AI00881; AI; NIAID; AI22974; AI; NIAID; AI23435; AI; NIAID; +

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Pyelonephritis-associated pili (Pap) are important in the pathogenesis of ascending, unobstructive Escherichia coli-caused renal infections because these surface bacterial organelles mediate digalactoside -specific binding to host uroepithelial cells. Pap are composed of many different polypeptides, of which only the tip proteins mediate specific binding. The PapA moiety polymerizes to form the bulk of the pilus structure and has been employed in vaccines despite its lack of Gal alpha(1-4)Gal receptor specificity. Animal recipients of PapA pilus -based vaccines are protected against experimental pyelonephritis caused by homologous and heterologous Gal - Gal -binding uropathogenic E. coli strains. Specific PapA immunoglobulin G antibodies in urine are correlated with protection in these infection models. The nucleotide sequences of the gene encoding PapA were determined for three E. coli clones expressing F7(1), F7(2), and F9 pili and were compared with corresponding sequences for other F serotypes. Specific rabbit antisera were employed in enzyme-linked immunosorbent assays to study the cross-reactivity between Gal - Gal pili purified from recombinant strains expressing F7(1), F7(2), F9, or F13 pili and among 60 Gal - Gal -binding wild-type strains. We present data which corroborate the concept that papA genes are highly homologous and encode proteins which exhibit greater than 70% homology among pili of different serotypes. The differences primarily occur in the cysteine-cysteine loop and variable regions and constitute the basis for serological diversity of these pili . Although there are differences in primary structures among these pili , antisera raised against pili of one serotype cross-reacted frequently with many other Gal - Gal pili of different serotypes. Furthermore, antisera raised against pili of the F13 serotype cross-reacted strongly or moderately with 52 (86%) of 60 wild-type Gal - Gal -binding E. coli strains. These data suggest that there are common immunogenic domains among these proteins. These additional data further support the hypothesis that broadly cross-protective PapA pilus vaccines for the immunoprophylaxis of pyelonephritis might be developed.

Record Date Created: 19911127

47/7/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06836082 91147196 PMID: 1671776
Alpha-hemolysin contributes to the pathogenicity of piliated digalactoside -binding Escherichia coli in the kidney: efficacy of an alpha-hemolysin vaccine in preventing renal injury in the BALB/c mouse model of pyelonephritis.
O'Hanley P ; Lalonde G; Ji G
Department of Medicine, Stanford University, California 94305.
Infection and immunity (UNITED STATES) Mar 1991, 59 (3) p1153-61, ISSN 0019-9567 Journal Code: 0246127
Contract/Grant No.: AI23435; AI; NIAID
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Digalactoside -binding (Gal - Gal) pili and alpha-hemolysin of Escherichia coli have been implicated as important virulence determinants in the pathogenesis of human ascending, nonobstructive pyelonephritis. The pathogenic significance of these determinants was evaluated in vitro and in the BALB/c mouse pyelonephritis model by employing wild-type, avirulent laboratory, and genetically defined cosmids, transformants, and recombinant strains. In vitro data suggest that the cytolytic activity of hemolysin is significantly (P less than 0.05) enhanced among digalactoside -binding strains which agglutinate erythrocytes. The basis of increased hemolysis is related presumably to more efficient delivery of the toxin to target lipid substrate in the host plasma membrane. Intravesicular administration of bacteria that express both digalactoside binding and hemolysin generally resulted in greater mortality and renal parenchymal injury in mice than strains that expressed none or only one of these determinants. Analyses convincingly demonstrate that digalactoside -binding pili are correlated with upper urinary tract colonization and that hemolysin is correlated with septicemia and renal parenchymal damage. These determinants collectively constitute the minimal virulence factors to produce disease in this model. Their efficacy as vaccines for the prevention of pyelonephritis was also assessed. A purified Gal - Gal pilus vaccine prevented (P less than 0.05) subsequent colonization by a challenge wild-type strain that exhibited homologous pili . The hemolysin vaccine did not abrogate subsequent bacterial renal colonization on challenge, but it did protect (P less than 0.05) mice which survived challenge from subsequent renal injury compared with those in the saline control group. The combination of these determinants was also protective. The combination of Gal - Gal pili and hemolysin in a vaccine preparation represents a potentially worthwhile strategy for human immunoprophylaxis against pyelonephritis by interdicting several steps in the pathogenesis of a bacterial mucosal infection.
Record Date Created: 19910402

47/7/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06445449 90136085 PMID: 2575704
Upstream activating sequences that are shared by two divergently transcribed operons mediate cAMP-CRP regulation of pilus -adhesin in Escherichia coli.

Goransson M; Forsman P; Nilsson P; Uhlin B E
Department of Microbiology, University of Umea, Sweden.
Molecular microbiology (ENGLAND) Nov 1989, 3 (11) p1557-65, ISSN 0950-382X Journal Code: 8712028
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Transcription of the genes encoding pilus -adhesin of serotype F13 in digalactoside -binding Escherichia coli required activation by the cAMP-CRP complex. Analysis of protein-DNA interaction in vitro showed that CRP bound in a cAMP-dependent manner to a sequence located 0.2 kb upstream of the point of transcription initiation of the pilus subunit operon. The cAMP-CRP activation included, in addition to the main pilus operon, the oppositely oriented operon encoding the PapI regulatory protein. Furthermore, the auto-regulatory product of the promoter-proximal gene (papB) in the pilus subunit operon was found to stimulate the papI transcriptional unit. Thus the cAMP-CRP complex and PapB might act in concert and indirectly promote pili synthesis by stimulating expression of the PapI positive regulator. The results of trans-complementation experiments and analyses using lacZ operon fusion derivatives showed that the cAMP-CRP activation also operated directly in cis on the pilus subunit operon. The region containing the CRP binding site appeared to function as an upstream activating sequence since deletion abolished expression even when the pap regulatory proteins PapI and PapB were supplied in trans. The implications for possible mechanisms of transcriptional activation by the cAMP-CRP complex at this novel location between the two oppositely oriented operons are discussed.

Record Date Created: 19900307

47/7/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06342482 90036691 PMID: 2572580
PapD, a periplasmic transport protein in P- pilus biogenesis.
Lindberg F; Tennent J M; Hultgren S J; Lund B; Normark S
Department of Microbiology, University of Umea, Sweden.
Journal of bacteriology (UNITED STATES) Nov 1989, 171 (11) p6052-8, ISSN 0021-9193 Journal Code: 2985120R
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

The product of the papD gene of uropathogenic Escherichia coli is required for the biogenesis of digalactoside -binding P pili . Mutations within papD result in complete degradation of the major pilus subunit, PapA , and of the pilinlike proteins PapE and PapF and also cause partial breakdown of the PapG adhesin. The papD gene was sequenced, and the gene product was purified from the periplasm. The deduced amino acid sequence and the N-terminal sequence obtained from the purified protein revealed that PapD is a basic and hydrophilic peripheral protein. A periplasmic complex between PapD and PapE was purified from cells that overproduced and accumulated these proteins in the periplasm. Antibodies raised against this complex reacted with purified wild-type P pili but not with pili purified from a papE mutant. In contrast, anti-PapD serum did not react with purified pili or with the culture fluid of piliated cells. However,

this serum was able to specifically precipitate the PapE protein from periplasmic extracts, confirming that PapD and PapE were associated as a complex. It is suggested that PapD functions in P- pilus biogenesis as a periplasmic transport protein. Probably PapD forms complexes with pilus subunits at the outer surface of the inner membrane and transports them in a stable configuration across the periplasmic space before delivering them to the site(s) of pilus polymerization.
Record Date Created: 19891215

47/7/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06170952 89255972 PMID: 2566625
Gal - Gal pili vaccines prevent pyelonephritis by piliated Escherichia coli in a murine model. Single-component Gal - Gal pili vaccines prevent pyelonephritis by homologous and heterologous piliated E. coli strains.
Pecha B; Low D; O'Hanley P
Veterans Administration Medical Center, Palo Alto, California 94304.
Journal of clinical investigation (UNITED STATES) Jun 1989, 83 (6) p2102-8, ISSN 0021-9738 Journal Code: 7802877
Contract/Grant No.: AI-23348; AI; NIAID; AI-23435; AI; NIAID; AI-2974; AI ; NIAID; +
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The initial pathogenic step in nonobstructive Escherichia coli pyelonephritis usually involves the binding of a bacterial adhesin with host uroepithelial glycoprotein receptors containing the D-Gal p alpha 1----4 D-Gal p beta 1 (Gal - Gal) moiety. In this study, groups of mice were immunized with Gal - Gal pili and challenged 2 wk later intravesicularly with E. coli strains expressing homologous or heterologous pili . 63 of 129 pili -immunized mice (49%) were protected from subsequent E. coli renal colonization compared with 5 of 85 control mice (6%). Among mice that had E. coli cultured from their right kidney, control mice had greater bacterial colony counts than pili -immunized animals (P less than 0.05). Light microscopic examination of kidneys demonstrated less histopathology among pili immunized mice than among control mice (P less than 0.05). Protection correlated with the presence of specific IgG antibodies in the urine and serum that bind to the major pilin structural polypeptide and not to the Gal - Gal pili tip adhesin per se. These results support the concept that immunization with a bacterial surface-coat constituent can prevent mucosal infection by interfering with colonization. Also Gal - Gal pili of E. coli represent a suitable candidate for immunoprophylaxis against pyelonephritis.
Record Date Created: 19890712

47/7/6 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05893130 88330182 PMID: 2901403
Isolation and comparison of Escherichia coli strains from canine and human patients with urinary tract infections.
Low D A; Braaten B A; Ling G V; Johnson D L; Ruby A L

RBIL5

Department of Pathology, University of Utah Medical Center, Salt Lake City 84132.

Infection and immunity (UNITED STATES) Oct 1988, 56 (10) p2601-9, ISSN 0019-9567 Journal Code: 0246127

Contract/Grant No.: AI23348; AI; NIAID

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

We analyzed Escherichia coli strains isolated from dogs with urinary tract infections (UTIs) in an attempt to determine if any of these strains were similar to E. coli isolated from humans with UTIs. Using genotypic and phenotypic traits, we identified four canine and six human E. coli UTI isolates that all appeared to be closely related or identical. All isolates shared similar DNA sequences for pyelonephritis-associated pili (pap), alpha-hemolysin (hly), and insertion sequence 5 (IS5), on the basis of Southern blot analysis. Similar outer membrane protein, pilin, and plasmid profiles were obtained for each of the isolates, although minor heterogeneity was observed. All of these isolates expressed a neuraminidase-sensitive binding phenotype in contrast to the majority of human isolates, which are known to express an adhesin that recognizes terminal digalactoside residues. Taken together, these results suggest that similar E. coli uropathogens may be capable of infecting both dogs and humans. To determine if the intestinal tracts of dogs were a reservoir for uropathogenic E. coli, eight paired rectal and urine pap+ E. coli strains were cultured from dogs with UTIs. By using the same genotypic and phenotypic criteria described above as a basis for strain identity, seven of eight urine-rectal pairs showed intrapair identity. However, each urine-rectal pair displayed a unique overall profile and could be distinguished from the other pairs. We conclude that the uropathogen colonizing the bladders of dog can also be the predominant strain colonizing the intestinal tracts.

Record Date Created: 19881026

47/7/7 (Item 7 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05769193 88216160 PMID: 2897064

Nucleotide sequence, regulation and functional analysis of the papC gene required for cell surface localization of Pap pili of uropathogenic Escherichia coli.

Norgren M; Baga M; Tennent J M; Normark S

Department of Microbiology, University of Umea, Sweden.

Molecular microbiology (ENGLAND) Sep 1987, 1 (2) p169-78, ISSN 0950-382X Journal Code: 8712028

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

The papC gene of uropathogenic Escherichia coli is required for the formation of digalactoside -binding Pap pili . papC forms part of an operon wherein the regulatory gene papB, the major pilin gene papA , a minor pilin-like gene papH, and papC are co-transcribed. Furthermore, the extent of PapC synthesis was found to affect the number of pili expressed on the cell surface. The DNA sequence of the papC gene is presented and its deduced amino acid sequence is compared to that of the FaeD protein encoded

by the K88 pili gene cluster. The PapC protein was localized to the E. coli outer membrane where it may form a trans-membrane channel through which pilin subunits are surface localized.
Record Date Created: 19880616

47/7/8 (Item 8 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05701098 88125013 PMID: 2448796
Synthetic peptides corresponding to protective epitopes of Escherichia coli digalactoside -binding pilin prevent infection in a murine pyelonephritis model.
Schmidt M A ; O'Hanley P ; Lark D; Schoolnik G K
Department of Medicine, Stanford University School of Medicine, CA 94305.
Proceedings of the National Academy of Sciences of the United States of America (UNITED STATES) Feb 1988, 85 (4) p1247-51, ISSN 0027-8424
Journal Code: 7505876
Contract/Grant No.: AI22974; AI; NIAID
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Synthetic peptides corresponding to five segments of a globoside (Gal - Gal)-binding pilin sequence [residues 5-12 (R5-12), R65-75, R93-104, R103-116, and R131-143], cyanogen bromide fragment II (CNBr-II, R53-163), and purified, intact Gal - Gal pili were prepared as vaccines and tested for their efficacy in a BALB/c murine model of pyelonephritis. Intact Gal - Gal pili , CNBr-II, and synthetic peptides R5-12 and R65-75 engendered antibodies that bound the homologous pilin protein and prevented urine and renal colonization in most vaccine recipients. Protection correlated with serum anti- pilus IgG ELISA titers greater than or equal to 1:250. The efficacy afforded by synthetic peptides R5-12 and R65-75 in vaccinated mice indicates that linear "antigenic" determinants in separate cyanogen bromide fragments encode "protective" epitopes. Peptides R93-104, R103-116, and R131-143 lacked efficacy, indicating that not all regions of the sequence are serologically equivalent. The crossreactivity of the peptide antisera for different Gal - Gal pilins was also assessed and correlated with the sequence homology of the corresponding regions. Antiserum to peptide R65-75, which corresponds to a region of unconserved sequence in heterologous pilins, bound only the homologous pilin. Thus, it specifies a type-specific protective epitope. Antiserum to synthetic peptide R5-12, which corresponds to a region of conserved sequence, bound Gal - Gal pilins from seven of eight pyelonephritis strains, indicating that it specifies a crossreacting protective epitope.
Record Date Created: 19880321

Q11N.26

47/7/9 (Item 9 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05549893 87289709 PMID: 2886993
The PapG protein is the alpha-D-galactopyranosyl-(1----4)-beta-D-galactopyranose-binding adhesin of uropathogenic Escherichia coli.
Lund B; Lindberg F; Marklund B I; Normark S
Proceedings of the National Academy of Sciences of the United States of America (UNITED STATES) Aug 1987, 84 (16) p5898-902, ISSN 0027-8424

Q11N.26

Journal Code: 7505876
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Uropathogenic Escherichia coli adhere to uroepithelial cells by their digalactoside alpha-D-galactopyranosyl-(1----4)-beta-D-galactopyranose [alpha-D-Galp-(1----4)-beta-D-Galp or Gal alpha (1----4)Gal]-binding pili , which are composed of repeating identical subunits. The major subunit (PapA) of these pili is not required for binding, but the papF and papG gene products are essential for adhesion. Transcomplementation analysis between the pap gene cluster and a related gene cluster encoding a different binding specificity showed that PapG and not PapF is the Gal alpha (1----4)Gal-specific adhesin. Antibodies against PapG were obtained upon immunizing with whole Pap pili , showing that the adhesin is a pilus component. Antisera specific for different Pap proteins were used to demonstrate that a pilin protein, either PapA or PapE, together with both PapG and PapF, must be exposed on the cell surface to allow E. coli to bind. The DNA sequence of the papG gene is presented, and the deduced primary structure showed similarities both to the B-chain sequence of the digalactoside -binding Shigella toxin and to established amino acid sequences of pilins.
Record Date Created: 19870918

47/7/10 (Item 10 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05506321 87258211 PMID: 2885755
Localization of the receptor-binding protein adhesin at the tip of the bacterial pilus .
Lindberg F; Lund B; Johansson L; Normark S
Nature (ENGLAND) Jul 2-8 1987, 328 (6125) p84-7, ISSN 0028-0836
Journal Code: 0410462
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Strains of the bacterium Escherichia coli that cause infections of the human urinary tract produce so-called Pap- pili , which are hair-like appendages consisting of about 10(3) helically arranged subunits of the protein PapA . These pili mediate binding to digalactoside -containing glycolipids present on the epithelial cells which line the urinary tract. Recently, it has been suggested that three proteins, PapE, PapF and PapG, are responsible for this binding. In the absence of PapA , non-piliated bacteria are formed which nonetheless exhibit binding, showing that the bulk of the pilus is not essential for binding. Although pili can form without PapF and PapG, such pili are unable to bind to the digalactoside . The protein PapG mediates binding specificity in trans-complementation experiments, so this protein is the digalactoside -specific adhesin. Using immuno-electron microscopy we have found that Pap- pili are heteropolymers composed of the major pilin, PapA , the minor pilins, PapE and PapF, and the adhesin, PapG. The last three proteins are located at the tip of the pilus .
Record Date Created: 19870731

Q11.N

47/7/11 (Item 11 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05438148 87187619 PMID: 2882856
Biogenesis of E. coli Pap pili : papH, a minor pilin subunit involved in cell anchoring and length modulation.
Baga M; Norgren M; Normark S
Cell (UNITED STATES) Apr 24 1987, 49 (2) p241-51, ISSN 0092-8674
Journal Code: 0413066
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The biogenesis of Escherichia coli Pap pili , encoded by the pap gene cluster, was studied. A novel gene, papH, was identified and found to encode a weakly expressed pilin-like protein. PapH was dispensable for digalactoside -specific binding and for formation of Pap pili . However, in papH deletion mutants 50%-70% of total pilus antigen was found free of the cells. We present evidence showing coregulation of papH and the adjacent gene, papA , which encodes the major pilin subunit. A decrease in the PapA to PapH ratio resulted in a large fraction of cells producing shortened pili ; whereas overproduction of PapA relative to PapH resulted in cells with lengthened pili . The data show that PapH has roles in anchoring the pilus to the cell and in modulating pilus length.
Record Date Created: 19870529

47/7/12 (Item 12 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

04793501 85166219 PMID: 2858852
Adhesion to human cells by Escherichia coli lacking the major subunit of a digalactoside -specific pilus -adhesin.
Uhlin B E; Norgren M; Baga M; Normark S
Proceedings of the National Academy of Sciences of the United States of America (UNITED STATES) Mar 1985, 82 (6) p1800-4, ISSN 0027-8424
Journal Code: 7505876
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Pathogenic bacteria frequently possess pili with specific binding properties that allow them to attach to epithelial tissue. In Escherichia coli, the pili associated with pyelonephritis (Pap pili) bind to digalactoside -containing glycolipids on the uroepithelium. Transposon-insertion mutants and deletion mutants of the cloned genetic determinant encoding synthesis of such digalactoside -binding Pap pili have been studied in E. coli K-12. Mutants that completely lack synthesis of the major Pap pili subunit protein, the papA gene product, and thereby no longer produce pili were shown to retain the binding specificity of intact Pap pili . Reduced expression of some of the remaining pap genes, presumably due to polarity effects from papA ::Tn5 insertions , was circumvented by the use of a copy-number mutant plasmid vector. Derivatives carrying the papA -D genes produced Pap pili but did not bind to human cells. The products of the genes papE-G are essential for digalactoside -specific hemagglutination and for attachment to urinary bladder cells. The papC and papD genes presumably aid in surface localization and/or

polymerization of the pili -adhesin subunits and are required for expression of pili as well as of the binding properties. Serological evidence is presented that suggests that a minor pilus component(s), presumably produced by the papE, -F, or -G gene, is the actual binding moiety in the digalactoside -specific interaction of Pap pilus -adhesin.
Record Date Created: 19850503

47/7/13 (Item 13 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

04779558 85159416 PMID: 2580037
Gal - Gal pyelonephritis Escherichia coli pili linear immunogenic and antigenic epitopes.
Schmidt M A ; O'Hanley P ; Schoolnik G K
Journal of experimental medicine (UNITED STATES) Apr 1 1985, 161 (4) p705-17, ISSN 0022-1007 Journal Code: 2985109R
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The linear immunogenic and antigenic structure of E. coli Gal - Gal pili from the recombinant strain HU 849 was investigated with nine synthetic peptides corresponding to regions of the pilus sequence predicted to contain hydrophilic beta-turns. Five peptides, as bovine serum albumin conjugates, were found by anti-HU 849 pilus serum and were thus designated "immunogenic epitopes." Peptides corresponding to R 25-38, R 38-50, and R 48-61 (which jointly comprise the single intramolecular disulfide loop), and R 103-116, were bound in low titer. A prominent immunogenic epitope was specified by a peptide corresponding to R 65-75. Four peptides, as thyroglobulin conjugates, elicited antisera in rabbits that bound intact HU 849 pili . These were designated "antigenic epitopes." Two prominent antigenic epitopes were localized to peptides corresponding to R 5-12 and R 93-104, whereas peptides corresponding to R 65-75 and R 119-131 represented two minor antigenic epitopes. None of the peptide antisera bound Gal - Gal pili from heterologous strains except anti-R 93-104 and anti-R 5-12. In 8 of the 10 Gal - Gal -binding pyelonephritis isolates tested, anti-R 5-12 detected a protein with an apparent molecular weight of 18,000 co-migrating with several Gal - Gal pili . Anti-R 93-104 detected a corresponding protein in 4 of 8 fecal and 7 of 12 pyelonephritis Gal - Gal -binding isolates; however, it also bound apparently unrelated proteins of higher molecular weight.
Record Date Created: 19850513

47/7/14 (Item 14 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

04749276 85131736 PMID: 2857730
Molecular basis of Escherichia coli colonization of the upper urinary tract in BALB/c mice. Gal - Gal pili immunization prevents Escherichia coli pyelonephritis in the BALB/c mouse model of human pyelonephritis.
O'Hanley P ; Lark D; Falkow S; Schoolnik G
Journal of clinical investigation (UNITED STATES) Feb 1985, 75 (2) p347-60, ISSN 0021-9738 Journal Code: 7802877
Contract/Grant No.: AI-18719; AI; NIAID
Document type: Journal Article

Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Most human pyelonephritis Escherichia coli isolates express both mannose (MS)- and globoside (Gal - Gal)-binding pili . An ascending E. coli urinary tract infection model was established in the 16-wk-old female BALB/c mouse to compare the pathogenic significance of MS and Gal - Gal pili and their efficacy as vaccines for the prevention of pyelonephritis. The distribution and density of pilus receptor compounds in urogenital tissues and as soluble compounds in urine were determined with antibodies to the synthetic receptor analogues, alpha D-Gal(1----4) beta D-Gal and alpha D-Man(1----2) alpha D-Man. Both carbohydrates were detected in vagina, bladder, ureter, and renal pelvis epithelium and in collecting duct and tubular cells. A pilus receptor compound also was detected in urine. It competitively inhibited the binding capacity of MS pili and was found to be physically, chemically, and immunologically related to Tamm-Horsfall uromucoid. Infectivity and invasiveness were quantitatively and histologically characterized for four E. coli strains: J96, a human pyelonephritis strain that expresses both MS and Gal - Gal pili ; two recombinant strains prepared from J96 chromosomal DNA encoding MS pili or Gal - Gal pili ; and the nonpiliated K12 recipient. Intravesicular administration of J96 (10(6) colony-forming units [CFU]) resulted in renal colonization and invasion in each of nine mice. The Gal - Gal clone (10(6) CFU) colonized the kidneys in each of 10 mice but did not invade. In contrast, the MS clone (10(6) CFU) did not colonize renal epithelium or invade. This effect was superceded when larger doses (greater than or equal to 10(10) CFU) of the MS clone were administered in volumes that cause acute vesicoureteric reflux. The efficacy was determined of vaccines composed of pure MS or Gal - Gal pili or the lipopolysaccharide containing O somatic antigen of the challenge strain, J96. The Gal - Gal pilus vaccine blocked renal colonization in 19 of 22 mice and renal invasion in 10 of 11 mice. Gal - Gal pili may be useful immunogens for the prevention of pyelonephritis in anatomically normal urinary tracts.

Record Date Created: 19850403

47/7/15 (Item 15 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

04546298 84236115 PMID: 6145590

Genes of pyelonephritogenic E. coli required for digalactoside -specific agglutination of human cells.

Lindberg F P; Lund B; Normark S

EMBO journal (ENGLAND) May 1984, 3 (5) p1167-73, ISSN 0261-4189
Journal Code: 8208664

Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Most pyelonephritic Escherichia coli strains bind to digalactoside -containing glycolipids on uroepithelial cells. Purified Pap pili (pili associated with pyelonephritis) show the same binding specificity. A non-polar mutation early in the papA pilin gene abolishes formation of Pap pili but does not affect the degree of digalactoside -specific hemagglutination. Three novel pap genes, papE , papF and papG are defined in this report. The papF and papG gene products are both required for digalactoside -specific agglutination by whole bacteria cells as well as

for agglutination by pilus preparations. Pili prepared from a papE mutant have lost their binding ability although whole cells from this mutant retain it, implying an adhesin anchoring role for the papE gene product. A mutant with lesions both in the papA and the papE genes does not mediate digalactoside -specific agglutination. The implications of this finding for pilus biogenesis are discussed.
Record Date Created: 19840807

47/7/16 (Item 16 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

04369424 84034918 PMID: 6195290
Mannose-sensitive and Gal - Gal binding Escherichia coli pili from recombinant strains. Chemical, functional, and serological properties.
O'Hanley P ; Lark D; Normark S; Falkow S; Schoolnik G K
Journal of experimental medicine (UNITED STATES) Nov 1 1983, 158 (5) p1713-19, ISSN 0022-1007 Journal Code: 2985109R
Contract/Grant No.: AI-18719; AI; NIAID
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Chromosomal genes encoding the MS and Gal - Gal binding properties have been cloned into separate recombinants and their respective pili characterized. Hapten inhibition of hemagglutination with synthetic carbohydrate receptor analogues and carbohydrate-adsorbed latex agglutination studies indicate that Gal - Gal and MS pili collectively exhibit the binding properties of the parent strain. MS pili migrated in SDS-PAGE with an Mr of 19 kdaltons and 17 kdaltons; the Mr of Gal - Gal pili was 17.5 kdaltons. The pili are chemically similar by amino acid composition and when the N-terminal cysteines are aligned, 8 of the 13 residues between positions 9 and 22 are homologous. Further, carboxy-terminal sequence homology was inferred from the carboxypeptidase digestion of a MS pili and the sequence of a carboxy-terminal tryptic peptide from Gal - Gal pili .
Record Date Created: 19831217

47/7/17 (Item 17 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

04297406 83289635 PMID: 6136465
Genetics of digalactoside -binding adhesin from a uropathogenic Escherichia coli strain.
Normark S; Lark D; Hull R; Norgren M; Baga M; O'Hanley P ; Schoolnik G; Falkow S
Infection and immunity (UNITED STATES) Sep 1983, 41 (3) p942-9, ISSN 0019-9567 Journal Code: 0246127
Contract/Grant No.: AI10885; AI; NIAID; AI14740; AI; NIAID; AI18462; AI; NIAID
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The uropathogenic strain Escherichia coli J96 mediates mannose-resistant hemagglutination owing to production of a digalactoside -binding adhesin.

A cosmid clone from this strain has been isolated that, when harbored in E. coli K-12, expressed Pap pili and this adhesin (R. Hull et al., Infect. Immun. 33:933-938, 1981). By transposon mutagenesis and by the construction of a number of hybrid plasmid derivatives, we have demonstrated that about 8.5 kilobases of DNA is required to generate a mannose-resistant hemagglutination-positive phenotype in E. coli K-12 strain P678-54. The structural gene for the Pap pili monomer, papA , has been identified and mapped close to the promotor-proximal end of the Pap operon. Although strain P678-54 that harbored a Tn5 insertion within papA showed a mannose-resistant hemagglutination-positive phenotype, it was negative in a competitive enzyme-linked immunosorbent assay with anti-Pap pilus serum. This could mean that a Pap adhesin is encoded by a region on the Pap operon that is distinct from papA .
Record Date Created: 19831021

47/7/18 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08739519 BIOSIS NO.: 199395028870
Reduced environment redox potential affects both transcription and expression of the pap pili gene.
AUTHOR: Maluszynska G M(a); Magnusson K-E; Rosenquist A
AUTHOR ADDRESS: (a)Dep. Med. Microbiol., Fac. Health Sci., Univ. Linkoping, S-581 85 Linkoping**Sweden
JOURNAL: Microbial Ecology in Health and Disease 5 (5):p257-267 1992
ISSN: 0891-060X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Pyelonephritis-associated pili (pap) gene expression is subject to a phase variation control mechanism by which cells alternate between two pili -expression states, viz. a 'phase-off' (pili -) and a 'phase-on' (pili +) state. During interaction with a host, Escherichia coli encounter various environmental redox conditions. We have addresses the question of whether bacteria are able to respond to this environmental signal by regulating pap pili biogenesis, a crucial colonisation factor in pyelonephritis. Transcription from the PapB promoter (papBAp) was studied in the Salmonella typhimurium papBAp lac fusion lysogen strain under aerobic, microaerobic and anaerobic conditions. In this strain, the beta-galactosidase gene is under the control of the papB promoter that initiates transcription of both the papb gene encoding the regulatory papB protein and the papA gene encoding the structural pili protein. The frequency of switching form the Lac+ (papBAp 'on') to the Lac- (papBAp 'off') state was about 1.3-fold higher when the environmental redox potential was reduced by changing from aerobic to microaerobic and anaerobic growth milieus. The beta-galactosidase activity representing the rate of transcriptional initiation from the papB promoter was, as calculated per 10-8 Lac+ bacteria, more than 12-fold higher in aerobically cultivated bacteria than in bacteria cultured under microaerobic or anaerobic conditions. Pap pili adhesin expression was measured under the same redox conditions, using E. coli K12 HB101 pPap 5 containing a plasmid coding for whole pap pili operon. The strongest pap pili expression, measured as agglutination of latex gal - gal beads, was observed under microaerobic

conditions similar to those found in the urinary tract. Under anaerobic conditions like those prevalent in the intestine, pap pili expression was negligible. This is not surprising, since such expression would not represent an ecological advantage for E. coli. In fact, repression of these types of fimbriae under anaerobic conditions may be a way in which the bacteria can save energy which can then be used to promote growth. Although the two genetic models used for transcription and expression studies are distinct, a high rate of transcription did not seem to correlate with optimal pili expression. This may include the importance of the post-transcriptional processing in pap pili expression.

47/7/19 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

06903868 BIOSIS NO.: 000089047940
UPSTREAM ACTIVATING SEQUENCES THAT ARE SHARED BY TWO DIVERGENTLY TRANSCRIBED OPERONS MEDIATE CYCLIC AMP CRP REGULATION OF PILUS -ADHESIN IN ESCHERICHIA-COLI
AUTHOR: GORANSSON M; FORSMAN K; NILSSON P; UHLIN B E
AUTHOR ADDRESS: DEP. MICROBIOL., UNIV. UMEA, S-901 87 UMEA, SWEDEN.
JOURNAL: MOL MICROBIOL 3 (11). 1989. 1557-1566. 1989
FULL JOURNAL NAME: Molecular Microbiology
CODEN: MOMIE
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Transcription of the genes encoding pilus -adhesin of serotype F13 in digalactoside -binding Escherichia coli required activation by the cAMP-CRP complex. Analysis of protein-DNA interaction in vitro showed that CRP bound in a cAMP-dependent manner to a sequence located 0.2 kb upstream of the point of transcription initiation of the pilus subunit operon. The cAMP-CRP activation included, in addition to the main pilus operon, the oppositely oriented operon encoding the PapI regulatory protein. Furthermore, the autoregulatory product of the promoter-proximal gene (papB) in the pilus subunit operon was found to stimulate the papI transcriptional unit. Thus the cAMP-CRP complex and PapB might act in concert and indirectly promote pili synthesis by stimulating expression of the PapI positive regulator. The results of trans-complementation experiments and analyses using lacZ operon fusion derivatives showed that the cAMP-CRP activation also operated directly in cis on the pilus subunit operon. The region containing the CRP binding site appeared to function as an upstream activating sequence since deletion abolished expression even when the pap regulatory proteins PapI and PapB were supplied in trans. The implications for possible mechanisms of transcriptional activation by the cAMP-CRP complex at this novel location between the two oppositely oriented operons are discussed.

47/7/20 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

06868685 BIOSIS NO.: 000089018276
PAP-D A PERIPLASMIC TRANSPORT PROTEIN IN P- PILUS BIOGENESIS
AUTHOR: LINDBERG F; TENNENT J M; HULTGREN S J; LUND B; NORMARK S

AUTHOR ADDRESS: DEP. MOL. MICROBIOL., WASHINGTON UNIV., ST. LOUIS, MO. 63130.
JOURNAL: J BACTERIOL 171 (11). 1989. 6052-6058. 1989
FULL JOURNAL NAME: Journal of Bacteriology
CODEN: JOBAA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The product of the papD gene of uropathogenic Escherichia coli is required for the biogenesis of digalactoside -binding P pili . Mutations within papD result in complete degradation of the major pilus subunit, PapA , and of the pilinlike proteins PapE and PapF and also cause partial breakdown of the PapG adhesin. The papD gene was sequenced, and the gene product was purified from the periplasm. The deduced amino acid sequence and the N-terminal sequence obtained from the purified protein revealed that PapD is a basic and hydrophilic peripheral protein. A periplasmic complex between PapD and PapE was purified from cells that overproduced and accumulated these proteins in the periplasm. Antibodies raised against this complex reacted with purified wild-type P pili but not with pili purified from a papE mutant. In contrast, anti-PapD serum did not react with purified pili or with the culture fluid of piliated cells. However, this serum was able to specifically precipitate the PapE protein from periplasmic extracts, confirming that PapD and PapE were associated as a complex. It is suggested that PapD functions in P- pilus biogenesis as a periplasmic transport protein. Probably PapD forms complexes with pilus subunits at the outer surface of the inner membrane and transports them in a stable configuration across the periplasmic space before delivering them to the site(s) of pilus polymerization.

47/7/21 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

06740365 BIOSIS NO.: 000088049795
GAL - GAL PILI VACCINES PREVENT PYELONEPHRITIS BY PILIATED ESCHERICHIA-COLI IN A MURINE MODEL SINGLE-COMPONENT GAL - GAL PILI VACCINES PREVENT PYELONEPHRITIS BY HOMOLOGOUS AND HETEROLOGOUS PILIATED ESCHERICHIA-COLI STRAINS
AUTHOR: PECHA B; LOW D; O'HANLEY P
AUTHOR ADDRESS: VETERANS ADM. MED. CENT., 3801 MIRANDA AVE., PALO ALTO, CALIF. 94304.
JOURNAL: J CLIN INVEST 83 (6). 1989. 2102-2108. 1989
FULL JOURNAL NAME: Journal of Clinical Investigation
CODEN: JCINA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

RBIC5

ABSTRACT: The initial pathogenic step in nonobstructive Escherichia coli pyelonephritis usually involves the binding of a bacterial adhesin with host uroepithelial glycoprotein receptors containing the D-Gal p.alpha. 1 .fwdarw. 4 D-Gal p.beta.1 (Gal - Gal) moiety. In this study, groups of mice were immunized with Gal - Gal pili and challenged 2 wk later intravesicularly with E. coli strains expressing homologous orheterologous pili . 63 of 129 pili -immunized mice (49%) were protected from subsequent E. coli renal colonization compared with 5 of

85 control mice (6%). Among mice that had E. coli cultured from their right kidney, control mice had greater bacterial colony counts than pili -immunized animals (P < 0.05). Light microscopic examination of kidneys demonstrated less histopathology among pili immunized mice than among control mice (P 7L 0.05). Protection correlated with the presence of specific IgG antibodies in the urine and serum that bind to the major pilin structural polypeptide and not to the Gal - Gal pili tip adhesin per se. These results support the concept that immunization with a bacterial surface-coat constituent can prevent mucosal infection by interfering with colonization. Also Gal - Gal pili of E. coli represent a suitable candidate for immunoprophylaxis against pyelonephritis.

47/7/22 (Item 5 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

06250462 BIOSIS NO.: 000086084644
BIOGENESIS OF ESCHERICHIA-COLI PAP PILI PAPH A MINOR PILIN SUBUNIT INVOLVED IN CELL ANCHORING AND LENGTH MODULATION
AUTHOR: BAGA M; NORGREN M; NORMARK S
AUTHOR ADDRESS: DEP. MICROBIOL., UNIV. UMEA, S-901 87 UMEA, SWEDEN.
JOURNAL: CELL 49 (2). 1987. 241-252. 1987
FULL JOURNAL NAME: Cell
CODEN: CELLB
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The biogenesis of Escherichia coli Pap pili , encoded by the pap gene cluster, was studied. A novel gene, papH, was identified and found to encode a weakly expressed pilin-like protein. PapH was dispensable for digalactoside -specific binding and for formation of Pap pili . However, in papH deletion mutants 50%-70% of total pilus antigen was found free of the cells. We present evidence showing coregulation of papH and the adjacent gene, papA , which encodes the major pilin subunit. A decrease in the PapA to PapH ratio resulted in a large fraction of cells producing shortened pili , whereas overproduction of PapA relative to PapH resulted in cells with lengthened pili . The data show that PapH has roles in anchoring the pilus to the cell and in modulating pilus length.

47/7/23 (Item 6 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

06224254 BIOSIS NO.: 000086058436
FUNCTIONAL AND STRUCTURAL HOMOLOGY AMONG REGULATORY CISTRONS OF PILI -ADHESIN DETERMINANTS IN ESCHERICHIA-COLI
AUTHOR: GORANSSON M; FORSMAN K; UHLIN B E
AUTHOR ADDRESS: DEP. MICROBIOL., UNIV. UMEA, S-90187 UMEA, SWEDEN.
JOURNAL: MOL GEN GENET 212 (3). 1988. 412-417. 1988
FULL JOURNAL NAME: Molecular & General Genetics
CODEN: MGGEA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Expression of the digalactoside -binding Pap pili involves two trans-acting regulatory genes, papB and papI. Using pap-lac operon fusion and DNA hybridization probes derived from pap DNA we tested whether or not other pili -adhesin determinants from different Escherichia coli strains encode homologs to the pap regulatory genes. Digalactose-specific clones of serotypes F72 and F11 complemented papB and papI mutants of the Pap (serotype F13) clone and DNA hybridization analysis showed that the clones are homologous in the DNA sequences encoding the two regulatory genes. Similar results were obtained with an S- pili determinant which mediates binding to sialic acid-containing receptors and the findings suggest that the regulatory regions may be more conserved than other genes in different pili -adhesion gene clusters. Determinants for type 1- pili (mannose-specific binding) and for pili associated with enterotoxigenic E. coli (K88, K99, CFAI, CFAII) did not appear to contain DNA sequences homologous to pap B or papI. E. coli strain J96, which was the origin of the pap DNA, was found to carry two additional copies of papB-papI homologous sequences in the chromosome. In strains expressing more than one kind of pili the trans-active gene products thereby may allow for regulatory interaction between separate pili -adhesin gene systems.

47/7/24 (Item 7 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

05759191 BIOSIS NO.: 000084107598
THE PAP-G PROTEIN IS THE ALPHA-D
GALACTOPYRANOSYL-1-4-BETA-D-GALACTOPYRANOSE-BINDING ADHESION OF UROPATHOGENIC ESCHERICHIA-COLI
AUTHOR: LUND B; LINDBERG F; MARKLUND B-I; NORMARK S
AUTHOR ADDRESS: DEP. MICROBIOL., UNIV. UMEA, S-901 87 UMEA, SWEDEN.
JOURNAL: PROC NATL ACAD SCI U S A 84 (16). 1987. 5898-5902. 1987
FULL JOURNAL NAME: Proceedings of the National Academy of Sciences of the United States of America
CODEN: PNASA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Uropathogenic Escherichia coli adhere to uroepithelial cells by their digalactoside .alpha.-D-galactopyranosyl-(1 .fwdarw. 4)-.beta.-D-galactopyranose [a-D-Galp-(1 .fwdarw. 4)-.beta.-D-Galp or Gal.alpha.(1 .fwdarw. 4)Gal], binding pilli, which are composed of repeating identical subunits. The major subunit (PapA) of these pili is not required for binding, but the papF and papG gene products are essential for adhesion. Transcomplementation analysis between the pap gene cluster and a related gene cluster encoding a different binding specificity showed that PapG and not PapF is the Gal.alpha. (1 .fwdarw. 4)Gal-specific adhesin. Antibodies against PapG were obtained upon immunizing with whole Pap pili , showing that the adhesin is a pilus component. Antisera specific for different Pap proteins were used to demonstrate that a pilin protein, either PapA or PapE, together with both PapG and PapF, must be exposed on the cell surface to allow E. coli to bind. The DNA sequence of the papG gene is presented, and the deduced primary structure showed similarities both to the B-chain sequence of the digalactoside -binding Shigella toxin and to establish amino acid

sequences of pilins.

47/7/25 (Item 8 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

05312765 BIOSIS NO.: 000032035894
IMPORTANCE OF GAL - GAL BINDING IN THE PATHOGENESIS OF ESCHERICHIA-COLI PYELONEPHRITIS A GAL - GAL PILUS VACCINE PREVENTS PYELONEPHRITIS IN BALB-C MICE
AUTHOR: O'HANLEY P ; SCHMIDT M A ; LARK D; SCHOOLNIK G
AUTHOR ADDRESS: DEP. MED., DIV. INFECTIOUS DISEASES, STANFORD UNIV., STANFORD, CALIF. 94305.
JOURNAL: BROWN, F., R. M. CHANOCK AND R. A. LERNER (ED.). NEW APPROACHES TO IMMUNIZATION: DEVELOPING VACCINES AGAINST PARASITIC, BACTERIAL, AND VIRAL DISEASES; CONFERENCE ON VACCINES 86, COLD SPRING HARBOR, N.Y., USA. XXI+418P. COLD SPRING HARBOR LABORATORY: COLD SPRING HARBOR, N.Y., USA. ILLUS. PAPER. ISBN 0-87969-190-5. 0 (0). 1986. 191-204. 1986
CODEN: 24608
RECORD TYPE: Citation
LANGUAGE: ENGLISH

47/7/26 (Item 9 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

04700602 BIOSIS NO.: 000080003727
MOLECULAR BASIS OF ESCHERICHIA-COLI COLONIZATION OF THE UPPER URINARY TRACT IN BALB-C MICE GLOBOSIDE-BINDING PILI IMMUNIZATION PREVENTS ESCHERICHIA-COLI PYELONEPHRITIS IN THE BALB-C MOUSE MODEL OF HUMAN PYELONEPHRITIS
AUTHOR: O'HANLEY P ; LARK D; FALKOW S; SCHOOLNIK G
AUTHOR ADDRESS: DEP. MED., DIV. INFECTIOUS DISEASES, STANFORD UNIV. MED. SCH., STANFORD, CALIF. 94305.
JOURNAL: J CLIN INVEST 75 (2). 1985. 347-360. 1985
FULL JOURNAL NAME: Journal of Clinical Investigation
CODEN: JCINA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Most human pyelonephritis E. coli isolates express both mannose (MS)- and globoside (Gal [galactose]-Gal)-binding pili . An ascending E. coli urinary tract infection model was established in the 16 wk old female BALB/c mouse to compare the pathogenic significance of MS and Gal - Gal pili and their efficacy as vaccines for the prevention of pyelonephritis. the distribution and density of pilus receptor compounds in urogenital tissues and as soluble compounds in urine were determined with antibodies to the synthetic receptor analogs, .alpha.D-Gal(1.fwdarw.4).beta.D-Gal and .alpha.D-Man mannose (1.fwdarw.2).alpha.D-Man. Both carbohydrates were detected in vagina, bladder, ureter and renal pelvis epithelium and in collecting duct and tubular cells. A pilus receptor compound also was detected in urine. It competitively inhibited the binding capacity of MS pili and was found to be physically, chemically and immunologically related to Tamm Horsfall uromucoid. Infectivity and invasiveness were quantitatively and

histologically characterized for 4 E. coli strains: J96, a human pyelonephritis strain that expresses both MS and Gal - Gal pili ; 2 recombinant strains prepared from J96 chromosomal DNA encoding MS pili or Gal - Gal pili ; and the nonpiliated K12 recipient. Intravesicular administration of J96 (106 colony-forming units [CFU]) resulted in renal colonization and invasion in each of 9 mice. The Gal - Gal clone (106 CFU) colonized the kidneys in each of 10 mice but did not invade. The MS clone (106 CFU) did not colonize renal epithelium or invade. This effect was superceded when larger doses (.gtoreq. 1010 CFU) of the MS clone were administered in volumes that cause acute vesicoureteric reflux. The efficacy was determined of vaccines composed of pure MS or Gal - Gal pili or the lipopolysaccharide containing O somatic antigen of the challenge strain, J96. The Gal - Gal pilus vaccine blocked renal colonization in 19 of 22 mice and renal invasion in 10 of 11 mice. Gal - Gal pili may be useful immunogens for the prevention of pyelonephritis in anatomically normal urinary tracts.

47/7/27 (Item 10 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

04536201 BIOSIS NO.: 000029059238
PATHOGENESIS OF ESCHERICHIA-COLI URINARY TRACT INFECTION
AUTHOR: LOW D; NORMARK S; SCHOOLNIK G; LARK D; O'HANLEY P ; FALKOW S
AUTHOR ADDRESS: DEP. MED. MICROBIOL., VETERANS ADM. HOSP., STANFORD UNIV., STANFORD, CALIF. 94305.
JOURNAL: AGABIAN, N. AND H. EISEN (ED.). UCLA (UNIVERSITY OF CALIFORNIA LOS ANGELES) SYMPOSIA ON MOLECULAR AND CELLULAR BIOLOGY NEW SERIES, VOL. 13. MOLECULAR BIOLOGY OF HOST-PARASITE INTERACTIONS; SELECTED PAPERS FROM THE MEETING, PARK CITY, UTAH, USA, JAN. 30-FEB. 4, 1983. XIX+351P. ALAN R. LISS, INC.: NEW YORK, N.Y., USA. ILLUS. ISBN 0-8451-2612-1. 0 (0). 1984 (RECD. 1985). 313-320. 1984
CODEN: USMBD
RECORD TYPE: Citation
LANGUAGE: ENGLISH

47/7/28 (Item 11 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

04337422 BIOSIS NO.: 000078066966
GENES OF PYELO NEPHRITOGENIC ESCHERICHIA-COLI REQUIRED FOR DI GALACTOSIDE SPECIFIC AGGLUTINATION OF HUMAN CELLS
AUTHOR: LINDBERG F P; LUND B; NORMARK S
AUTHOR ADDRESS: DEP. MICROBIOL., UNIV. UMEA, S-901 87 UMEA, SWEDEN.
JOURNAL: EMBO (EUR MOL BIOL ORGAN) J 3 (5). 1984. 1167-1174. 1984
FULL JOURNAL NAME: EMBO (European Molecular Biology Organization) Journal
CODEN: EMJOD
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Three novel pap genes, papE, papF and papG are defined. The papF and papG gene products were both required for digalactoside -specific agglutination by whole bacteria cells and for agglutination by pilus preparations. Pili prepared from a papE mutant had no binding ability;

whole cells from this mutant retained it, implying an adhesin anchoring role for the papE gene product. A mutant with lesions in the papA and the papE genes did not mediate digalactoside -specific agglutination. The implications of this finding for pilus biogenesis are discussed.

47/7/29 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

05578740 EMBASE No: 1993346840
Pap pili as a vector system for surface exposition of an immunoglobulin G- binding domain of protein A of Staphylococcus aureus in Escherichia coli
Steidler L.; Remaut E.; Fiers W.
Laboratory of Molecular Biology, Gent University, K.L. Ledeganckstraat 35,B-9000 Ghent Belgium
Journal of Bacteriology (J. BACTERIOL.) (United States) 1993, 175/23 (7639-7643)
CODEN: JOBAA ISSN: 0021-9193
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

MICRO

Fusion genes between papA , the gene coding for the major Pap pilus subunit, and fragments coding for an immunoglobulin G-binding domain of the Staphylococcus aureus protein A were constructed in such a way that the spa fragments were inserted following either codon 7 or 68 of the coding sequence for the mature portion of PapA . Peptides in the area of amino acids 7 and 68 of PapA are localized at the external side of the pilus. A set of p(L) expression plasmids containing papA and derivatives suitable for insertion were constructed. A papA gene carrying a spa insert following codon 68 was cloned back into the pap operon. The presence of this altered operon in a bacterial strain allowed the detection of immunoglobulin G-binding activity at the surfaces of the bacterial cells.

47/7/30 (Item 1 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

135343274 CA: 135(24)343274w PATENT
Immunogenic pili presenting foreign peptides: vaccination against urinary tract infections
INVENTOR(AUTHOR): Denich, Kenneth; Schmidt, M. Alexander
LOCATION: USA
ASSIGNEE: O'Hanley, Peter
PATENT: PCT International ; WO 200179277 A2 DATE: 20011025
APPLICATION: WO 2001US11918 (20010412) *US PV196491 (20000412)
PAGES: 35 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: C07K-014/195A; C07K-014/245B; A61K-039/02B; C12N-015/10B; C12N-015/66B; A61P-013/02B
DESIGNATED COUNTRIES: AE; AG; AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; BZ; CA; CH; CN; CO; CR; CU; CZ; DE; DK; DM; DZ; EE; ES; FI; GB; GD; GE; GH; GM; HR; HU; ID; IL; IN; IS; JP; KE; KG; KP; KR; KZ; LC; LK; LR; LS; LT; LU; LV; MA; MD; MG; MK; MN; MW; MX; MZ; NO; NZ; PL; PT; RO; RU; SD; SE; SG; SI; SK; SL; TJ; TM; TR; TT; TZ; UA; UG; UZ; VN; YU; ZA; ZW; AM; AZ; BY; KG; KZ; MD; RU; TJ; TM DESIGNATED REGIONAL: GH; GM; KE; LS; MW; MZ; SD; SL; SZ; TZ; UG ; ZW; AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; TR; BF; BJ; CF; CG; CI; CM; GA; GN; GW; ML; MR; NE; SN; TD; TG

SECTION:
CA215002 Immunochemistry
CA210XXX MICROBIAL, ALGAL, AND FUNGAL BIOCHEMISTRY
CA214XXX Mammalian Pathological Biochemistry
IDENTIFIERS: papH pilin Escherichia urinary infection vaccine, immunogen papA pilin Escherichia vaccine
DESCRIPTORS:
Bladder...
cystitis; papH deletion mutants and chimeric papA proteins in vaccination against P-pilus bacteria and urinary tract infection
Peptides,biological studies...
epitopes of papA of uropathogenic Escherichia coli
Plasmid vectors...
for expression of papH deletion mutants and chimeric papA proteins of uropathogenic Escherichia coli
Pilins...
gene papA; papH deletion mutants and chimeric papA proteins in vaccination against P-pilus bacteria and urinary tract infection
Pilins...
gene papH; papH deletion mutants and chimeric papA proteins in vaccination against P-pilus bacteria and urinary tract infection
Urinary tract...
infection; papH deletion mutants and chimeric papA proteins in vaccination against P-pilus bacteria and urinary tract infection
Epitopes...
of papA of uropathogenic Escherichia coli
Pilus...
P-; papH deletion mutants and chimeric papA proteins in vaccination against P-pilus bacteria and urinary tract infection
Kidney,disease...
pyelonephritis; papH deletion mutants and chimeric papA proteins in vaccination against P-pilus bacteria and urinary tract infection
Vaccines...
synthetic; papH deletion mutants and chimeric papA proteins in vaccination against P-pilus bacteria and urinary tract infection
Escherichia coli...
uropathogenic; papH deletion mutants and chimeric papA proteins in vaccination against P-pilus bacteria and urinary tract infection
CAS REGISTRY NUMBERS:
369596-64-5D papA fusion products, papH deletion mutants and chimeric papA proteins in vaccination against P-pilus bacteria and urinary tract infection
96886-16-7 369596-65-6 369596-66-7 369596-67-8 369596-68-9 369596-69-0 369596-70-3 369596-71-4 369596-72-5 369596-73-6 369596-74-7 papH deletion mutants and chimeric papA proteins in vaccination against P-pilus bacteria and urinary tract infection
152256-57-0 153272-93-6 153272-94-7 370655-05-3 370655-06-4 370655-07-5 370655-08-6 370655-09-7 370655-10-0 370655-11-1 370655-12-2 370655-13-3 370655-14-4 370655-15-5 370655-16-6 unclaimed sequence; immunogenic pili presenting foreign peptides, vaccination against urinary tract infections

47/7/31 (Item 2 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

106152847 CA: 106(19)152847b JOURNAL
Regulation and biogenesis of digalactoside-binding pili
AUTHOR(S): Uhlin, Bernt Eric; Baaga, Monica; Forsman, Kristina; Goeransson, Mikael; Lindberg, Frederik; Lund, Bjoern; Norgren, Mari; Normark, Staffan
LOCATION: Dep. Microbiol., Univ. Umea, Umea, Swed.
JOURNAL: FEMS Symp. DATE: 1986 VOLUME: 31 NUMBER: Protein-Carbohydr. Interact. Biol. Syst. PAGES: 13-18 CODEN: FEMSDW ISSN: 0163-9188
LANGUAGE: English
SECTION:
CA210004 Microbial Biochemistry
IDENTIFIERS: pili digalactoside binding gene papA
DESCRIPTORS:
Pili...
digalactoside-binding, formation and regulation of, genetics in relation to
Gene and Genetic element,microbial, papB... Gene and Genetic element,microbial, papE...
for pili formation, regulation of
Galactosides,di-...
pili binding, formation of, genetics in relation to

47/7/32 (Item 3 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

104116077 CA: 104(14)116077a PATENT
Vaccine against urinary infection
INVENTOR(AUTHOR): O'Hanley, Peter; Falkow, Stanley; Schoolnik, Gary K.; Lark, David
LOCATION: USA
ASSIGNEE: Leland Stanford Junior University
PATENT: European Pat. Appl. ; EP 161095 A2 DATE: 851113
APPLICATION: EP 85303016 (850429) *US 605287 (840430)
PAGES: 29 pp. CODEN: EPXXDW LANGUAGE: English CLASS: A61K-039/108A; A61K-037/02B DESIGNATED COUNTRIES: AT; BE; CH; DE; FR; GB; IT; LI; LU; NL; SE
SECTION:
CA163003 Pharmaceuticals
CA115XXX Immunochemistry
IDENTIFIERS: urinary infection vaccine Escherichia pilin
DESCRIPTORS:
Vaccines...
against urinary infection, contg. Escherichia coli HU849 pilin
Urinary tract...
infections of, vaccine against, contg. antigenic determinant sequences of Escherichia coli Gal-Gal pilus protein
Pilins...
of Escherichia coli HU849, as vaccine, against urinary tract infections
Protein sequences...
of pilin, from Escherichia coli HU849
Escherichia coli...
pilin of HU849, as vaccine against urinary infection
CAS REGISTRY NUMBERS:
100644-86-8 100644-87-9 100663-35-2 100754-45-8 antigenic determinant
in Escherichia coil pilus protein, vaccines, for treatment of urinary

tract infections
100785-33-9 vaccines, for treatment of urinary tract infections

47/7/33 (Item 1 from file: 351)
DIALOG(R)File 351:Derwent WPI

014213642
WPI Acc No: 2002-034340/200204
Novel immunogenic composition useful for preventing and treating urinary tract infection or other microbial infections/diseases, comprises dissociated pili from Gal - Gal binding pilus -producing bacteria
Patent Assignee: DENICH K (DENI-I); O'HANLEY P (OHAN-I); SCHMIDT M A (SCHM-I); OHANLEY P (OHAN-I)
Inventor: DENICH K ; SCHMIDT M A
Number of Countries: 094 Number of Patents: 002
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 200179277	A2	20011025	WO 2001US11918	A	20010412	200204	B
AU 200151569	A	20011030	AU 200151569	A	20010412	200219	

Priority Applications (No Type Date): US 2000196491 P 20000412
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 200179277	A2	E	35	C07K-014/195	

Designated States (National): AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW

AU 200151569	A		C07K-014/195	Based on patent WO 200179277

Abstract (Basic): WO 200179277 A2

NOVELTY - An immunogenic composition (I) comprising dissociated pili from a Gal - Gal binding pilus -producing bacteria, where the pili comprises at least one immunogenic peptide inserted into the immunodominant region of PapA that does not normally contain the peptide, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a vaccine (II) for preventing urinary tract infections or other microbial infections /diseases, if a corresponding protective epitope is inserted into the immunodominant region of PapA , comprising (I);

(2) producing pili , by culturing a recombinant Gal - Gal pilus -producing bacteria, where the pili comprise at least one immunogenic peptide inserted into an immunodominant PapA region that does not normally contain the peptide, and recovering the dissociated pili ; and

(3) producing a vaccine, by formulating a vaccine comprising a pili produced by the above said method, or rendering protein based haptens immunogenic by the carrier effect of fusion with PapA sequences at this location.

ACTIVITY - Antibacterial; antimicrobial.

MECHANISM OF ACTION - Vaccine (claimed). The efficacy of purified

pili from each papH mutant was assessed in the standard experimental BALB/c model of pyelonephritis. Cohorts of 20 female mice (of 14 weeks old) were immunized intramuscularly on day 0 and day 14 with 50 mug of purified pili from each papH mutant. Each vaccinial administration consisted of 100 mul of pili -incomplete Freund's adjuvant emulsion. Mice were challenged intravesically on day 30 by 106 bacteria expressing the homologous pili antigen. Challenge strains included J96 for KD849-5 vaccine recipients, 3669 for KD2001-8 vaccine recipients, KD201 for KD201-8 vaccine recipients, and KD210B for KD210B-11 vaccine recipients. Protection against renal colonization by the challenge strain was assessed at day 2 after challenge. Positive controls included cohorts of 5 non-vaccinated mice challenged with each strain of bacteria. The pili vaccine conferred protection if the right renal homogenates did not reveal any bacterial growth in lesser than 90% of the cohort and none of the renal homogenates in the cohort had more than 5 colony forming units (CFU) per gram of tissue.

USE - (II) is useful for treating or preventing urinary infection or other microbial infections/diseases (claimed).

pp; 35 DwgNo 0/5

Derwent Class: B04; D16
International Patent Class (Main): C07K-014/195
International Patent Class (Additional): A61K-039/02; A61P-013/02; C07K-014/245; C12N-015/10; C12N-015/66

47/7/34 (Item 2 from file: 351)
DIALOG(R)File 351:Derwent WPI

004457840
WPI Acc No: 1985-284718/198546
Vaccines against urinary tract infections - contg. new E. coli gal - gal pilus protein or fragments
Patent Assignee: UNIV LELAND STANFORD JUNIOR (STRD)
Inventor: FALKOW S; LARK D; OHANLEY P; SCHOOLNIK G
Number of Countries: 015 Number of Patents: 005
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
EP 161095	A	19851113	EP 85303016	A	19850429	198546	B
AU 8541851	A	19851107				198601	
JP 61000022	A	19860106	JP 8594545	A	19850430	198607	
US 4736017	A	19880405	US 84605287	A	19840430	198816	
CA 1261550	A	19890926				198945	

Priority Applications (No Type Date): US 84605287 A 19840430
Cited Patents: 4.Jnl.Ref; A3...8722; EP 170496; EP 48881; EP 60499; No-SR.Pub; WO 8504654
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
EP 161095	A	E	29		

Designated States (Regional): AT BE CH DE FR GB IT LI LU NL SE

Abstract (Basic): EP 161095 A

(A) Pilus vaccines for treating urinary tract infections in humans contain a polypeptide with an amino acid sequence corresp. to at least one antigenic determinant of Gal - Gal pilus protein.

(B) E.coli HU849 Gal - Gal pilus protein (I), comprising a

sequence of 163 amino acid, and the 79-110, 15-70, 133-163 and 111-125 fragments of (I) are new.

(I) may be obtained by (a) isolation and purification from E. coli HU849 pili , (b) peptide synthesis, or (c) recombinant DNA technology using the appropriate DNA coding sequence.

ADVANTAGE - (I) and its fragments are highly effective and specific in generating antibodies to urinary pathogens and are obtainable in practical amts. and in pure form.

1/2

Abstract (Equivalent): US 4736017 A

Immunogenic peptide comprises at least 15 aminoacids of defined sequence, corresp. to one or more antigenic determinants of Escherichia coli Gal - Gal pilus protein.

USE - The prods. and their active fragments are dispersed with the usual pharmaceutical carriers and opt. additives to provide a vaccine which gives protection against urinary infections. (10pp

Derwent Class: B04; D16

International Patent Class (Additional): A61K-037/02; A61K-039/10; C07K-007/08; C07K-013/00; C07K-015/04; C12N-001/20

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